The New England
Journal of Medicine

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VOLUME 222 FEBRUARY 29, 1940 NUMBER 9

THE VALUE OF ROUTINE BLOOD-PROTEIN DETERMINATIONS*

Report of Results in 320 Consecutive Cases

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RECENT medical literature is replete with papers stressing the clinical importance of blood-protein determinations. Unfortunately the complexity of quantitative protein determinations has hindered the widespread use of this procedure.

Until recently the most widely used methods for blood-protein determinations included the macro- and micro-Kjeldahl, the colorimetric and the refractometric methods. These are complex procedures, relatively expensive as to equipment and to upkeep, and time-consuming even in the hands of experienced technicians. Both the clinician and the laboratory worker have long been in search of simpler methods. Several have been introduced and, though helpful, lacked quantitative accuracy.

The recently introduced Kagan[1, 2] method combined for the first time simplicity with the desired quantitative accuracy. This method is rapid, the apparatus is inexpensive and the technic can be readily mastered by any technician.

Kagan checked the accuracy of this method against the macro-Kjeldahl method and found the greatest deviation in 107 specimens to be 0.48 gm. per 100 cc., with a mean deviation of 0.16 gm. For clinical purposes such small deviations are irrelevant.

On the medical services of the Boston City Hospital it is customary to order blood-protein determinations only when specifically indicated, because the total number performed by the laboratory must necessarily be limited. The acquisition of a Kagan proteinometer by one of us (H. H. S.) suggested the idea of doing routine blood-protein determinations on a large series of consecutive admissions to the Fifth Medical Service. The present paper summarizes and discusses the results secured in 320 such cases.

METHOD AND PROCEDURE

The falling drop method for determination of specific gravity was first published by Barbour and Hamilton.[3] Moore and Van Slyke[4] later worked out the relation between plasma specific gravity and plasma protein content. Kagan, using this knowledge, devised a practical clinical test whereby the total protein of blood could be determined by noting the rate at which a drop of serum or plasma fell a measured distance through a mixture of synthetic methyl salicylate and heavy California mineral oil. The principle of this method is based on Stokes law and is described in Kagan's papers. A standardized apparatus for performing this test is now available commercially.§

The technic used in our study was as follows: the blood of 320 patients admitted to the Fifth Medical Service during April and May, 1939, was subjected to Kagan's test, the blood sample being collected at the same time as that for the routine Hinton test. Two cubic centimeters was placed in a small, dry test tube and centrifuged until the serum separated from the clot. The serum and proteinometer were allowed to remain at room temperature for ten minutes before using. Kagan's technic was followed. By means of a calibrated pipette 0.015 cc. (15 cu. mm.) of serum was introduced into the glass cylinder of the proteinometer, and the time required for the drop of serum to fall 10 cm. through the oil was measured to one-tenth of a second by means of a stopwatch. The protein value of the serum was obtained from a calibrated chart, due correction being made for the temperature of the oil. Most of the determinations required less than one minute for their completion, and all were made by one of us (H. H. S.). A dietary history, obtained by clinical clerks working on the service, was available in the majority

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§The Kagan proteinometer was obtained from E. H. Sargent & Co., Chicago.

of these cases. In 20 cases, blood was also submitted to the hospital chemical laboratory for protein determination by the Kjeldahl method.

Six to 8 gm. per 100 cc. is the commonly accepted normal variation for the total protein value in man, with the albumin-globulin ratio varying from 1.5 to 2.5.[5] Variations from normal include: hypoproteinemia (a total protein less than 6 gm. per 100 cc.), hyperproteinemia (a total protein over 8 gm. per 100 cc.), changes in the albumin-globulin ratio and, rarely, the presence of abnormal (Bence-Jones) protein. A shifted albumin-globulin ratio commonly accompanies the first two. Changes in the fibrinogen value, while too small to influence grossly the total value, are nevertheless important because of their effect on the sedimentation rate. The latter is said to be a rough index of the blood-fibrinogen value.[6]

Hyperproteinemia

For many years hyperproteinemia was little understood and but rarely detected. A recent review[7] of the literature showed that not only does the presence of hyperproteinemia have considerable diagnostic value, but its pathologic physiology accounts for many phenomena otherwise hard to explain. These may include the following changes in the blood: rouleaux formation, increased sedimentation rate, spontaneous precipitation of proteins, blood-protein precipitation by Hayem's solution while performing a red-blood-cell count, discrepancy in acid-base equivalence, failure of clot to retract, rapid coagulation, possible changes in osmotic pressure, anticomplementary Wassermann reactions, changes in viscosity and variation in isoelectric point.

In practically every case on record, the protein increase was in the globulin fraction, usually accompanied by an absolute diminution of albumin and a marked reversal of the albumin-globulin ratio. In rare cases, Bence-Jones protein or fibrinogen constituted the protein increase. Although protein values over 8.0 gm. per 100 cc. are stressed here, the same significance could be attached to values as low as 6.5 gm., provided evidence was obtained for marked reversal of the albumin-globulin ratio.

Table 1. *Common and Rare Causes of Hyperproteinemia.**

COMMON CAUSES	RARE CAUSES
Dehydration	Metastatic bone lesions
Multiple myeloma (60%)	Malaria
Lymphogranuloma inguinale (75%)	Still's disease
Subacute bacterial endocarditis (50%)	Erythema induratum (Bazin)
Leprosy (80%)	Syndrome of Bing and Neel[21]
Kala-azar (40%)	Early portal cirrhosis
Schistosomiasis (50%)	Syphilis
Boeck's sarcoid	Leukemia
	Filariasis
	Osteopathia osteopriva
	Tuberculosis
	Rheumatoid arthritis
	Trypanosomiasis

*The percentage values (based on a survey of the literature) represent the frequency with which hyperproteinemia is found in certain diseases.

Diagnostically, the finding of hyperproteinemia should suggest one of the conditions listed in Table 1.

Hypoproteinemia

Hypoproteinemia is considered present when the total blood-protein level falls below 6 gm. per 100 cc. Most commonly one finds the decrease to be due to the lowering of the albumin fraction, accompanied or followed by a relative increase in globulin and a reversal of the albumin-globulin ratio. That edema may develop when the total protein falls below 5 gm. per 100 cc. has been well demonstrated,[8] but unfortunately application of this knowledge in clinical practice is often lacking.

Table 2. *Causes of Hypoproteinemia.**

- Malnutrition:
  - Dietary:
    - Endemic and sporadic
    - Associated with chronic infection, pellagra and beriberi
  - Poor absorption:
    - Idiopathic
    - Diarrhea
    - Intestinal fistulas, ileostomy and so forth
    - Neoplasm of gastrointestinal tract
  - Poor utilization (?)
- Kidney diseases (with albuminuria):
  - Nephroses, all types
  - Glomerular nephritis, chronic
  - Amyloid kidney
- Liver diseases:
  - Cirrhosis
  - Extensive neoplasm
- Protein dilution:
  - Excess fluid administration
  - Fever
  - Hyperthyroidism
- Protein loss:
  - Hemorrhage, acute or chronic
  - Weeping wounds or skin lesions
  - Shock, surgical and traumatic
- Heart failure
- Chronic poisoning:
  - Benzene, carbon tetrachloride, phosgene, phosphorus and so forth
- Toxemias of pregnancy

*Based on Kagan's classification.[22]

In the past, the effect of hypoproteinemia on the formation or aggravation of edema has been of interest chiefly to the internist.

Recent articles[9–11] suggest, however, that the significance of hypoproteinemia is greater than is generally believed. It may interfere with proper wound healing.[10] It may slow gastrointestinal peristalsis to a degree suggestive of intestinal obstruction, especially after a gastroenterotomy.[11] Since it thus increases the difficulties of gastrointestinal operations, it is of more than theoretical interest to the abdominal surgeon.

Hypoproteinemia is common in hyperthyroidism. That it may necessitate a two-stage procedure and have a suggestive relation to postopera-

tive thyroid crisis brings the subject within the province of the thyroid surgeon.[12] The condition may be the responsible factor or at least aggravate certain types of toxemia of pregnancy, thus making the subject of interest to the obstetrician.[13] No doubt future studies will determine more fully the significance of hypoproteinemia.

The common causes of hypoproteinemia are given in Table 2. The complexities of this subject have been well reviewed by Melnick and Cowgill[14] and Moschcowitz,[15] and need no further comment here.

Results

A summary of the general results is shown in Table 3. In the group of 320 patients, 238 (74.5 per cent) had total protein determinations within the normal range of 6 to 8 gm. per 100 cc. Only 8 patients (3.3 per cent) had edema,* 6 of these presenting cases of cardiac decompensation.

TABLE 3. *Number and Percentage of Cases in Each Protein Range, with Number and Percentage Showing Edema.*

Protein Range	All Cases		Cases with Edema	
	No.	Per cent of total	No.	Per cent of group
gm. per 100 cc.				
Over 8.00	1	0.3	0	0
8.00–6.00	238	74.5	8	3
6.00–5.50	42	13.1	7	16
5.50–5.00	22	6.8	5	22
5.00 or less	17	5.3	7	41
Totals	320		27	

There were 42 patients (13.1 per cent) with total protein values ranging from 5.5 to 6.0 gm. per 100 cc., 7 of whom (16 per cent) had clinically recognizable edema.

Twenty-two patients (6.8 per cent) had total protein values in the range of 5.0 to 5.5 gm. per 100 cc., with 5 of them (22 per cent) showing edema. In only 1 case (a patient with avitaminosis) was there general anasarca. The diagnoses of patients in this group are given in Table 4, together with an estimate of the dietary intake of protein. In 4 cases the diet was considered to be adequate with regard to protein intake. Other mechanisms for producing hypoproteinemia in this group include poor absorption (cancer of colon), poor utilization (diabetes, acute and chronic infection) and heart failure.

TABLE 4. *Data from Cases with Blood-Protein Values of 5.00 to 5.50 Gm. per 100 Cc.*

Clinical Diagnosis	Blood Protein	Edema	Diet
	gm. per 100 cc.		
Diabetes mellitus	5.49	0	Inadequate
Tabes dorsalis	5.04	?*	?*
Lobar pneumonia	5.21	?	?
Pregnancy (7th month); bronchopneumonia	5.42	0	Adequate
Chronic sinusitis	5.49	0	?
Peripheral vascular disease	5.45	0	Adequate
Chronic alcoholism	5.35	+	Grossly inadequate
Lobar pneumonia	5.24	0	?
Mediastinal tumor	5.49	+++	?
Decompensated rheumatic heart disease	5.31	+++	?
Chronic alcoholism, beriberi	5.19	++++	Inadequate
Chronic alcoholism	5.40	0	Inadequate
Jacksonian epilepsy	5.35	0	Inadequate
Lobar pneumonia	5.31	0	?
Migraine	5.21	0	Adequate
Carcinoma of the colon	5.14	0	Inadequate
General avitaminosis	5.32	++++	Grossly inadequate
Duodenal ulcer	5.17	0	Inadequate
Acute tonsillitis	5.19	0	Inadequate
Pulmonary tuberculosis	5.35	0	Adequate
Chronic alcoholism	5.49	0	Inadequate
Bronchopneumonia	5.21	0	Inadequate

*Means that a specific statement was lacking in record.

Values of less than 5 gm. per 100 cc. were obtained for 17 patients (5.3 per cent). The relevant data are given in Table 5. The most significant finding was the presence of edema in 7 (41 per cent) of these patients, 4 of them showing marked edema of generalized distribution. Where available, the dietary history revealed a grossly inadequate protein intake in almost every case. Liver disease, infection, poor gastrointestinal absorption and utilization, loss of blood and heart disease were important additional factors producing hypoproteinemia in some of these cases. Two patients had clinically recognizable beriberi, 1 had the classical picture of scurvy, and 1 evidenced

TABLE 5. *Data from Cases with Blood-Protein Values below 5.00 Gm. per 100 Cc.*

Clinical Diagnosis	Blood Protein	Edema	Probable Reason for Hypoproteinemia
	gm. per 100 cc.		
Beriberi (polyneuritis), chronic alcoholism	4.90	++	Grossly inadequate diet
Portal cirrhosis, general avitaminosis	4.08	++++	Inadequate diet, liver disease
Chronic alcoholism, chronic bronchiectasis	4.90	0	Inadequate diet, chronic infection
Beriberi (polyneuritis), chronic alcoholism	4.83	++++	Grossly inadequate diet
Carcinoma of stomach	4.60	?	Anorexia, poor absorption
Advanced pulmonary tuberculosis	4.64	0	Chronic infection, anorexia
Psychogenic vomiting	4.87	0	Diet adequate but not retained
General avitaminosis, chronic alcoholism	4.73	0	Inadequate diet
Senility, bronchopneumonia	4.80	0	Infection, anorexia
Scurvy	4.83	++++	Grossly inadequate diet
Decompensated coronary heart disease	4.18	+++	Grossly inadequate diet
Decompensated rheumatic heart disease	4.55	+	Adequate diet (cause not determined)
Generalized arteriosclerosis, senility	4.97	0	Inadequate diet, anorexia
Carcinoma of large intestine	4.83	0	Inadequate diet, poor absorption
Bleeding peptic ulcer	4.69	0	Protein loss, poor diet
Idiopathic hypochromic anemia	4.93	++	Inadequate diet, poor absorption
Mucous colitis (7 years' duration)	4.93	0	Protein loss, poor absorption

*Edema here refers to peripheral pitting edema present on admission.

generalized vitamin deficiency. Less clear-cut evidence of deficiency — that is, dry or rough skin, stomatitis, glossitis, soft gums — was present in most of the other patients in this group, but such findings are naturally difficult to evaluate.

The large number of low protein values in our series suggested to us the necessity of checking the method in a group of healthy normal persons partaking of an adequate diet. Therefore, blood from 25 individuals (physicians, medical students, orderlies and technicians) was obtained and analyzed by the Kagan technic for total blood protein. The results are tabulated in Table 6. All,

TABLE 6. *Protein Values on Blood from 25 Normal Persons, Ages 24 to 35.*

BLOOD PROTEIN	NO. OF CASES
gm. per 100 cc.	
5.70–6.00	2
6.01–6.30	12
6.31–6.60	8
6.61–6.90	1
6.91–7.20	2

with 2 exceptions (5.93 and 5.70 mg. per 100 cc.) fell within the normal range. No adequate explanation for these two low values could be ascertained, the diet in each case being adequate. One could conclude that the low values for the hospital patients were not due to a tendency for this method to give low readings, but represent true cases of hypoproteinemia.

This is further shown to be true by comparing the 20 total blood-protein values obtained by the hospital chemical laboratory, where the standard

TABLE 7. *Comparison of Blood-Protein Values Obtained by the Falling-Drop Method with Those Obtained by Chemical Analysis.*

KAGAN FALLING-DROP METHOD	MACRO-KJELDAHL METHOD	MICRO-KJELDAHL METHOD	DEVIATION
gm. per 100 cc.	*gm. per 100 cc.*	*gm. per 100 cc.*	*gm. per 100 cc.*
6.18		6.3	+0.12
5.70		5.6	−0.10
6.11		6.4	+0.29
6.39		6.5	+0.11
5.63		5.9	+0.27
6.21		6.7	+0.49
6.18		6.0	−0.18
6.80	6.7		−0.10
5.90	6.0		+0.10
4.64	4.6		0.00
6.28	6.4		+0.12
6.00	6.0		0.00
5.97	6.1		+0.13
5.52	5.5		−0.01
5.49	5.4		0.00
6.14	6.1		0.00
6.97	6.5		0.47
6.69	6.7		+0.01
6.07	5.9		0.17
8.73	8.9		+0.17

macro- and micro-Kjeldahl methods are used, with those obtained by the Kagan technic. The figures are shown in Table 7. It can be seen that the greatest variation was 0.49 gm. per 100 cc., with an average deviation of 0.14 gm. Our results indicate clearly that the detailed chemical procedures are no more accurate for routine work than is the Kagan technic, and might well be dispensed with in any busy hospital laboratory.

In only 1 case was hyperproteinemia discovered, a value of 8.73 gm. per 100 cc. being obtained in a case of multiple myeloma. The formol-gel and Takata-Ara tests were strongly positive, which suggested, although the albumin-globulin ratio was not determined, that the globulin fraction was greatly increased. The main clue to the diagnosis in this case was the hyperproteinemia. Our results show that hyperproteinemia is considerably less common than hypoproteinemia, at least among the average run of medical cases seen in this district. On an active medical service one would be unlikely to find more than five or ten cases in the course of a year. The diagnostic significance of the condition is so great, however, that even the rare case is worthy of consideration.

It has been stressed that the protein level of 8 gm. per 100 cc. or over for the diagnosis of hyperproteinemia is only relative, for actually it is the presence of hyperglobinemia that is the more significant.[7] The Takata-Ara test is said to be positive when the globulin fraction is over 3 gm. per 100 cc.[16] and the formol-gel test usually positive when the globulin value reaches 4 gm.[17] For routine clinical work these simple laboratory procedures suffice to detect globulin increase and should be done along with the Kagan technic wherever possible. Only rarely will it be necessary to determine the globulin fraction by chemical analysis. Therefore, one should view any total protein of 7 gm. per 100 cc. or over with the same suspicion attached to values over 8 gm. per 100 cc., provided the albumin-globulin ratio proves to be reversed. It would perhaps be wisest to have every protein determination, regardless of its level, accompanied by some estimate of the globulin fraction.

COMMENT

It was a distinct surprise to find that almost 25 per cent of the patients in this series had a protein value below normal; 12.1 per cent of the determinations were less than 5.5 gm. per 100 cc., and 5.3 per cent were less than 5.0 gm. (the level commonly accepted as being clinically significant). Edema was distinctly commoner in the low-protein group, so much so, that in this hospital, at least, one would be justified in considering hypoproteinemia as the main, or at least a contributory, mechanism each time an edematous patient is studied. The difficulty of controlling cardiac decompensation in the presence of hypoproteinemia is particularly important,[18] and is probably

often overlooked. In other words, the presence of edema in any form indicates the necessity for determining the blood-protein level.

The influence of dehydration on the blood-protein level was not considered in our patients but is extremely important. It is common for very ill patients to be dehydrated on admission, thus increasing the total protein value of the blood. With restoration of the fluid to normal, subsequent determinations may show the blood protein to be diluted sufficiently to produce hypoproteinemia. Therefore, a true estimate of the blood-protein level cannot be secured until the fluid balance of the body has been restored to normal. This should be especially considered in those clinics where it is customary to take blood specimens immediately after the patient is admitted to the ward.

It is now generally accepted that few nutritional deficiencies occur singly. The discovery of one indicates the presence of others, even though not marked enough for clinical recognition. In this sense, the determination of the total blood-protein value is at present the easiest laboratory test available for detection of a dietary deficiency. The presence of hypoproteinemia indicates the need for a dietary history and a thorough search for the clinical minutiae suggestive of other deficiencies.

In our own series, abnormal protein values were found as commonly as significant deviations from normal in the routine urinalyses, blood nonprotein nitrogen and sugar determinations, blood counts, Hinton reactions and so forth.

In the past, technical difficulties discouraged follow-up studies on patients with abnormal protein values. This technic encourages such studies.

With regard to treatment, it is obvious that most persons with hypoproteinemia will respond favorably to dietary measures alone. However, the presence of liver disease and poor gastrointestinal absorption or utilization may preclude such a simple approach. Where necessary, intravenous therapy in the form of blood transfusion or, if available in the future for general human use, injections of lyophile serum[19] or aminoacids[20] would be indicated for temporarily increasing the blood-protein level. The latter methods have potentialities certain to stimulate further studies.

Summary

The blood-protein level for each of 320 medical patients and 25 controls was determined by the Kagan falling-drop technic. The method proved not only accurate but so simple that routine determinations were easily possible. Our results indicate that abnormal blood-protein values are commonly found on a general medical service. The significance of such changes has been briefly reviewed and discussed in the light of our results.

References

1. Kagan, B. M.: A simple method for the estimation of total protein content of plasma and serum. I. A falling-drop method for the determination of specific gravity. *J. Clin. Investigation* **17**:369-372, 1938.
2. *Idem:* A simple method for the estimation of total protein content of plasma and serum. II. The estimation of total protein content of human plasma and serum by the use of the falling-drop method. *J. Clin. Investigation* **17**:373-376, 1938.
3. Barbour, H. G., and Hamilton, W. F.: The falling-drop method for determining specific gravity. *J. Biol. Chem.* **69**:625-640, 1926.
4. Moore, N. S., and Van Slyke, D. D.: The relationships between plasma specific gravity, plasma protein content and edema in nephritis. *J. Clin. Investigation* **8**:337-355, 1930.
5. Cantarow, A., and Trumper, M.: *Clinical Biochemistry.* Second edition. 666 pp. Philadelphia: W. B. Saunders Co., 1939. P. 97.
6. Ham, T. H., and Curtiss, F. C.: Sedimentation rate of erythrocytes: influence of technical, erythrocyte and plasma factors and quantitative comparison of five commonly used sedimentation methods. *Medicine* **17**:447-517, 1938.
7. Jeghers, H., and Selesnick, S.: Hyperproteinemia: its significance. *Internat. Clin.* **3**:249-279, 1937.
8. Keefer, C. S.: Edema: Its pathologic physiology and clinical significance. *Internat. Clin.* **2**:85-102, 1933.
9. Barden, R. P.; Thompson, W. D.; Ravdin, I. S., and Frank, I. L.: The influence of the serum protein on the motility of the small intestine. *Surg., Gynec. & Obst.* **66**:819-821, 1938.
10. Thompson, W. D.; Ravdin, I. S., and Frank, I. L.: Effects of hypoproteinemia on wound disruption. *Arch. Surg.* **36**:500-508, 1938.
11. Mecray, P. M., Jr.; Barden, R. P., and Ravdin, I. S.: Nutritional edema: its effect on the gastric emptying time before and after gastric operations. *Surgery* **1**:53-64, 1937.
12. Bartels, E. C.: Serum-protein studies in hyperthyroidism. *New Eng. J. Med.* **218**:289-294, 1938.
13. Strauss, M. B.: Observations on the etiology of the toxemias of pregnancy. V. The etiologic relationship between water retention and arterial hypertension. *Am. J. M. Sc.* **196**:188-198, 1938.
14. Melnick, D., and Cowgill, G. R.: The problem of hypoproteinemia. *Yale J. Biol. & Med.* **10**:49-63, 1937.
15. Moschcowitz, E.: Hypoproteinemia. *J. A. M. A.* **100**:1086-1092, 1933.
16. Kirk, R. C.: The Takata-Ara test and its relation to cirrhosis of the liver. *J. A. M. A.* **107**:1354-1357, 1936.
17. Wise, C. R., and Gutman, A. B.: The formol-gel reaction: a convenient preliminary test for hyperglobulinemia. *Am. J. M. Sc.* **194**:263-270, 1937.
18. Ellis, L. B.: Plasma protein deficiency in patients with cardiac edema. *M. Clin. North America* **16**:943-949, 1933.
19. Thompson, W. D.; Ravdin, I. S.; Rhoads, J. E., and Frank, I. L.: Use of lyophile plasma in correction of hypoproteinemia and prevention of wound disruption. *Arch. Surg.* **36**:509-518, 1938.
20. Elman, R., and Weiner, D. O.: Intravenous alimentation, with special reference to protein (amino acid) metabolism. *J. A. M. A.* **112**:796-802, 1939.
21. Bing, J., and Neel, A. V.: Two cases of hyperglobulinaemia with affection of the central nervous system on toxi-infectious basis. *Acta. Med. Scandinav.* **88**:492-506, 1936.
22. Kagan, B. M.: personal communication.

SURGICAL PROBLEMS IN DIVERTICULITIS*

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BOSTON

BEFORE proceeding to a discussion of the surgical aspects of diverticulitis certain recognized facts relating to diverticulosis and to uncomplicated diverticulitis should be emphasized.

In the first place, diverticula seldom occur in people under forty and are most often found in obese men over that age. During routine gastrointestinal x-ray examinations diverticula are found in 3 to 10 per cent of patients. At the Massachusetts General Hospital, for example, in 6426 consecutive barium-enema examinations, they were revealed in 3 per cent of the cases. Of this percentage only a small number of persons are likely to develop diverticulitis to a degree which will bring them to a doctor and permit a definite diagnosis to be made. The sigmoid is the commonest site of diverticulum formation, and diverticula are also most numerous in this area — both factors decreasing as the cecum is approached. The sigmoid is likewise by far the most frequent site of diverculitis, even though the entire colon may be studded with diverticula. Diverticula without evidence of spasm by x-ray examination, and without clinical evidence of inflammation, need no treatment except encouragement of normal eating and bowel habits, in order to lessen the likelihood of diverticulitis. When inflammation does develop, the patient remains a medical problem unless complications of perforation or obstruction occur. In such an event, although operative procedures are not necessary in every case, the patient should be promptly observed by a surgeon, who can best assume the responsibility of deciding this point and carrying out the proper procedure. Finally, mild intermittent attacks of diverticulitis may go on for years without the occurrence of a perforation or of serious obstruction, while other cases are more fulminating and demand surgical procedures of varying number and degree.

Acute Diverticulitis

A patient during an acute attack, with fever, pain and a palpable, tender mass, usually in the left lower quadrant, inevitably has an associated period of obstipation, due to temporary swelling and obstruction in the sigmoid. Usually this situation does not demand surgery. Such an individual is best treated by rest in bed, morphine, the giving of fluids, freely by vein and in moderation by mouth, heat or cold applied locally for comfort, and abstention from the use of an enema until the process is definitely subsiding. Even then an enema should be given with extreme caution, using not over a pint of water, since perforation can be produced by fluid pressure. Mineral oil administered by mouth and by rectum in small amounts after four or five days is safe and of some benefit. No cathartics should be given. Under this type of treatment most cases will have subsided by the end of a week, the fever dropping, the pain lessening, the mass becoming less evident and bowel function re-establishing itself. On the other hand, persistence of or an increase in temperature, pain, tenderness and the size of the mass suggests the likelihood of a walled-off abscess from slow perforation, for which an operation will probably be necessary. It should also be remembered, however, that a small abscess resulting from perforation may establish spontaneous drainage into the bowel and recovery may ensue without operation. I have had at least 2 patients who were very sick for ten to fourteen days and in whom this unquestionably occurred, as determined later by barium enemas which revealed a perisigmoidal cavity in each.

It is a matter of considerable importance to decide rightly whether or not to explore a case of diverticulitis during an acute episode, and also to determine the best procedure after entering the abdomen.

I have reviewed the records of 140 cases of diverticulitis treated at the Massachusetts General Hospital by various surgeons from 1911 to 1936 inclusive, and also 35 cases from my own files. The figures in this paper, however, are based only on the former group. Of the 140 patients, 63 were operated on one or more times (Table 1), while 77 were treated without surgery. The number of operated cases in proportion to the total is, of course, much higher than would be true in a group of cases seen outside a hospital, since as a rule the sickest patients go to hospitals. Thus, in the 35 cases from my private practice, operative procedures were carried out in only 5 cases, or about 14 per cent of the total.

*Read at the annual meeting of the New England Surgical Society, Salem, Massachusetts, September 30, 1939.

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Exploration of Uncomplicated Cases

Of the 63 Massachusetts General Hospital cases submitted to operation, 12 were explored during an acute attack and a mass in the sigmoid without evidence of perforation was found. Of the 12 patients, 8 were sewed up without drainage and all recovered except 1, who died of peritonitis, due apparently to a perforation into the peritoneal cavity, which developed the day after operation. In the remaining 4 cases a drain was placed in the

TABLE 1. *Operative Procedures on 63 Patients.*

OPERATIVE PROCEDURE	NO. OF TIMES PERFORMED
Exploration, with or without drainage, in non-perforated cases	12
Exploration and drainage for sudden perforation with peritonitis	3
Exploration and drainage for slow perforation with abscess	14
Posterior colpotomy for pelvic abscess	3
Cecostomy	16
Colostomy (descending colon)	9
Colostomy (transverse colon)	10
Mikulicz resection	3
Resection with end-to-end suture	2
Anterior resection with permanent colostomy	4
Ileostomy	2
Exploration with resection of diverticulum	3
Total	81

neighborhood of the mass, and all the patients recovered. It would appear from these figures that drainage is unnecessary when no perforation is discovered at operation, even though there may be some exudate present. Likewise, in retrospect, a decision not to operate at all would have been proper, although in some cases there was evidently sufficient doubt as to the preoperative diagnosis so that exploration seemed advisable. Those cases of acute diverticulitis, in which, by virtue of the fact that the sigmoid lies near or to the right of the midline, a preoperative diagnosis of acute appendicitis is inescapable, demand immediate operation. Unnecessary exploration of uncomplicated cases should, however, be avoidable in most instances.

Sudden Perforation

A sudden perforation into the free peritoneal cavity is much less common than slow perforation; it occurred in only 3 of the 140 cases in this series. All 3 patients were operated on. One died of peritonitis and 1 recovered. The third case, in which perforation occurred after exploration, has been mentioned.

Slow Perforation with Abscess

In another group of 14 cases, abscesses developed from slow perforation, and were explored and drained through the peritoneal cavity, with a high mortality. Seven patients died in the hospital of peritonitis, while 7 recovered. One of the latter died later of carcinoma, which was probably present originally. The 7 deaths from peritonitis might have been avoided by a delay in operation until the abscess either drained spontaneously into the bowel or increased sufficiently in size to be accessible through the rectum or the vagina or beneath the abdominal wall. In this group of cases, a cecostomy was performed at the same time in 1 of the 7 fatal cases and in 1 of the 7 recovered cases, a fact which seems to indicate that such a procedure is an unnecessary adjunct to simple drainage under such circumstances.

Three other acute cases developed low-pelvic abscesses which were opened through the vagina; all the patients left the hospital, though 1 died two months later of sepsis.

CHRONIC OBSTRUCTIVE DIVERTICULITIS

Recurring attacks of acute inflammation in the same area eventually build up a chronically inflamed, thickened segment of bowel, which never returns to normal between the episodes. A narrowing of the lumen is continually present, though it may not be obvious on a liquid or low-residue diet except during the exacerbations of inflammation. The sigmoid may have become adherent to the bladder during one of these attacks, with or without the formation of a fistula; if a fistula is present, the subsequent attacks are associated with dysuria and frequency, and also with pneumaturia. Fistulas may develop between the colon and the small bowel, rectum, vagina or abdominal wall. In this series there were 4 cases with vesicocolic fistulas, all operated on more or less successfully by multiple stages. One nephrocolic and 1 enterocolic fistula occurred, the former patient dying without operation, the latter after attempted repair.

Indications for Colostomy

Not infrequently, individuals develop intestinal obstruction to a degree which necessitates surgical relief by colostomy. In such cases it is often difficult to be certain whether one is dealing with cancer or diverticulitis, not only prior to operation but also after the abdomen has been opened. Regardless of whether the incision has been made on the right or left side, exploration is likely to be difficult because of distention; the differential diagnosis frequently cannot be made by palpation of the mass and often is in doubt even when the mass is visualized. Furthermore, it is frequently undesirable even to attempt exploration of the mass in the presence of marked distention.

Diversion of the fecal stream will cause the diverticulitis to quiet down in all cases, but the chronic obstructive process never can return to normal, and subsequent closure of the colostomy

is likely to produce a recurrence of the trouble. In one of our cases a barium enema fifteen months after colostomy revealed little or no reduction in the narrowing; closure, despite this fact, resulted in death of the patient from peritonitis.

Indications for Resection

There are several factors justifying radical surgery in an increasing number of cases of chronic diverticulitis. These are recurring obstruction and fistula formation, the possibility of perforation during further acute attacks, and the ever-present possibility that the obstruction may actually be due to cancer rather than diverticulitis, or to a coexistence of both conditions. The ability of a good radiologist to differentiate the two lesions by detecting the loss of mucosa due to cancer is a great help to the surgeon in deciding for or against operation.

Types of Operative Procedure

Since obstruction occurs almost invariably in the sigmoid — usually in its upper part — and since it seldom involves over 10 cm. of bowel, it is possible in most cases to resect this segment and restore continuity, though a permanent colostomy will be necessary in some. Because of the inflammatory thickening of the mesosigmoid, which is often more prominent than is the thickening of the bowel itself, resection is more dangerous than in the case of cancer and should rarely be carried out as a single-stage procedure. A colostomy should precede resection.

Cecostomy, which diverts very little fecal material, is indicated only as the simplest method of relieving complete obstruction in a sick patient. It was performed in 16 cases in this series, with 1 death from peritonitis. In a number of these cases other procedures were also carried out, either before or after cecostomy.

Colostomy using the descending colon is ill-advised if future resection is contemplated, because the opening is situated too near the area of the second operation. Nevertheless, the descending colon was utilized in 9 cases in the series, with no operative mortality.

Complete diversion of the bowel contents is best accomplished by colostomy in the transverse colon, with section of the bowel. The two ends can be constructed for later closure either by the Mikulicz or the Devine method, the former being simpler, and probably just as efficient as the latter. Transverse colostomy was performed in 10 of our cases, with 1 death from pneumonia.

After several weeks' interval during which the defunctioned distal bowel is washed out daily, the obstructing segment can be resected and continuity re-established either by the Mikulicz method or by end-to-end suture, using basting stitches or an anastomosis clamp such as that devised by Young.* In a bowel cleaned out for several weeks, an open anastomosis can probably be done successfully, though the so-called "aseptic" methods are safer. A short, thick mesocolon, such as that found so often in heavy-set individuals, with its thickness increased by the chronic inflammation of diverticulitis, does not usually lend itself to a Mikulicz resection since the bowel is also short. Under these circumstances an end-to-end anastomosis is the only feasible procedure short of permanent colostomy.

In the Massachusetts General Hospital series, Mikulicz resection of the sigmoid was performed in 3 cases, all with good results. End-to-end suture was carried out in 2 cases, also successfully. Anterior resection, with a permanent colostomy and inversion of the rectal stump, was performed in 4 cases, with 2 hospital deaths from sepsis. Inversion of the stump is technically difficult as a rule, and if the stump is short it may not be possible to leave the inverted end within the peritoneal cavity without drainage, which is the best way to handle it. If the stump slips below the peritoneum, drainage should be carried out through the vagina or beside the coccyx; but even so, fatal retroperitoneal sepsis may occur.

Since it is impossible to know in advance which of the above procedures will prove to be best, and since resection with end-to-end suture without preliminary defunctioning of the left colon is risky, it is evident that a colostomy in the transverse colon should precede all resections of the left colon for diverticulitis and all attempts to disconnect and repair fistulas resulting from perforation.

Ileostomy was performed in 2 cases of the series, in one for gangrenous diverticulitis of the cecum and in the other to permit closure of a badly broken-down cecostomy stoma. Resection of a single diverticulum was carried out in 3 cases. Eighty-one operative procedures were performed in 63 patients.

End Results

I have been able thus far to secure adequate end-result data on 44 of the 77 unoperated cases and on 49 of the 63 operated cases, a total of 93 patients.

Of the 44 unoperated cases, 3 patients died in the hospital, and 14 died later. It developed that 2 of the latter group had cancer of the sigmoid as well as diverticulitis. In the other 12, death was also due to causes other than diverticulitis. Twenty-seven patients have remained alive for

*Young, F. L., Jr.: A new instrument for intestinal anastomosis. *New Eng. J. Med.* 206:943-945, 1932.

varying periods of time, 19 without symptoms and 8 with recurring attacks.

Of the 49 operated cases followed, 28 patients died. Sixteen of these died in the hospital. Of the 12 subsequent deaths, 5 were due to what was reported to be cancer of the colon, — though this was not proved in every case, — 4 to complications of the diverticulitis and 3 to unrelated causes. Twenty-one patients were still living, 5 with recurrent symptoms of diverticulitis and 16 apparently free from symptoms. Of the entire group of cases, 31 had only one operation while 18 were subjected to two or more surgical procedures.

Conclusions

Acute diverticulitis is always a nonsurgical problem unless perforation makes operation necessary.

Immediate operation is essential in a sudden acute perforation, while delayed operation is preferable in a slow perforation with abscess.

Chronic obstructive diverticulitis, with or without fistula formation, though relieved by complete diversion of the fecal contents, is likely to recur if the colostomy is closed. Resection, when the left colon has been rendered clean following colostomy, is a relatively safe procedure, and is usually indicated in these cases.

270 Commonwealth Avenue.

Discussion

Dr. John Homans, Boston: There is one aspect of this subject which I should like to speak of, and that is the type of infection which is apt to spread, especially into the retroperitoneal tissues. The effect is exceedingly dangerous and often fatal. Moreover, the intestinal bacteria may include the gas-forming organisms, and at the Peter Bent Brigham Hospital several years ago a surgeon, in exploring a thickening not known to be due to diverticulitis, examined and lifted the adherent sigmoid. In consequence the instruments became contaminated with the gas bacillus, and the patient and two others died before anyone suspected the possible presence of these bacteria. Of course ordinary scrubbing and boiling had failed to destroy their spores on the instruments.

Dr. William C. Quinby, Boston: A point which I think is worth noting, in regard to those communications which sometimes occur as a result of perforation of a diverticular abscess into the urinary bladder, is that in the majority of cases the opening formed is so small that it is rather hard to find by cystoscope; as a result, the infection is usually not one which causes a great deal of bladder dysfunction — not much pain and frequency of urination, but nevertheless a persistent pyuria.

In the cases which have been spoken of as showing pneumaturia and so forth, the communication into the bladder is usually, in my experience, the result of an intestinal cancer rather than simple peridiverticular abscess. In these cases the area of the perforation into the bladder is much more readily seen through the cystoscope than it is in cases of the former type.

Dr. Thomas H. Russell, New Haven, Connecticut: It happens that I have 2 cases at the present time in which an intestinal resection has been done for diverticulitis. One is that of a woman of sixty-six, who had a series of x-ray films taken eighteen months before which showed diverticula. She had an acute flare-up a few months before, and twenty-four hours before I saw her had an acute attack of vomiting. The leukocyte count was 23,000, and a mass was made out in Douglas's cul-de-sac. An operation was done ten days ago through a low midline incision. From the earlier x-ray films it was evident that the diverticula were very low. The upper portion of the rectum and the lower sigmoid were infiltrated with pus, and the patient was very sick. I was able to deliver the inflamed loop, part of which was gangrenous. The patient is now making normal progress.

Three days ago I saw a man of sixty-seven, who had had intermittent attacks of partial obstruction. It was decided to operate on him. A Mikulicz operation was more easily done in this case because the involved portion of the intestine was the sigmoid. I removed the loop of intestine yesterday, and anticipate a smooth convalescence.

These two cases which were resected have been the only ones in which I thought it necessary to do a radical operation, the others being treated conservatively or by simple drainage.

ANTEPARTUM GAS-BACILLUS INFECTION*

Report of a Case with Septicemia and Recovery But with Death of the Fetus

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THE presence of *Clostridium welchii* in the genital tract is not uncommon. While all true strains of *Cl. welchii* are probably pathogenic, the presence of this organism does not necessarily signify infection, because Schottmüller[1] found it in the vaginas of healthy women. Certain prerequisites are necessary for pathogenicity, namely trauma and tissue necrosis. Falls[2] noted the presence of *Cl. welchii* in 6.3 per cent of a large series of prenatal patients. At the Sloane Hospital in New York City, Bysshe[3] reported *Cl. welchii* in 25 out of 547 antepartum and postpartum patients, an incidence of 4.5 per cent. Of the 25 cases, 1 patient died presenting the typical picture of gas-bacillus sepsis, and 5 developed puerperal endometritis in which the only organism found was *Cl. welchii*. Peckham[4] in his study of 545 patients ill with puerperal infection found the organism in only 0.6 per cent of those cultured.

Cl. welchii is probably present in a larger number of infected cases than one realizes, and apparently is not at all times an organism of high virulence but only when circumstances are favorable. If it were virulent, undoubtedly there would be far more deaths attributable to such infection.

In 38,330 deliveries at the Margaret Hague Maternity Hospital, only 3 cases have been definitely diagnosed as complicated by *Cl. welchii* infections. In 1934 a patient had an intrauterine *Cl. welchii* infection diagnosed at delivery of a full-term baby. The patient had been seen by a midwife, who examined her several times vaginally at home. She was treated with serum and recovered. In 1935 another patient entered the hospital with a high temperature, was delivered of a stillbirth and died of a pelvic gas-bacillus infection within twenty-four hours. In the recovered case reported herewith the patient was proved to be infected systemically and locally with virulent *Cl. welchii*. There may have been other cases in which *Cl. welchii* was a factor in morbidity, but no other characteristic case in either mother or child has been noted. This fact, together with the known incidence of *Cl. welchii* in the flora of the birth tract, noted above, excites speculation as to the virulence of the organism and the conditioning factors.

We know that the organism is essentially a saprophyte, becoming pathogenic only when introduced into a tissue medium that fulfills the necessary prerequisites, that is, consists of tissue which is devitalized, dying or necrotic. De Kruif, Adams and Ireland[5] and De Kruif and Bollman[6] have amply demonstrated that the spores or vegetative organisms thoroughly washed free of toxin are far less virulent than are equal numbers of organisms not separated from the toxin. The primary conditions for infection are usually established by tissue damage resulting from wounds; areas of necrotic tissue furnish a favorable medium for the growth of the organism, making it possible for the bacilli to produce toxin, which eventually leads to toxemic injury and death.

In 49 cases with an abnormal pregnancy, labor or puerperium, Wrigley[7] found *Cl. welchii* in the lochia of 13 patients and drew the conclusion that this organism is usually exogenous. He postulated the following conditions as necessary in order to have severe maternal infection: the organisms must be introduced into the uterus; they must find there suitable "dead" material—the fetus—on which to grow; the dead fetus must remain in utero a sufficient time for active infection to begin; and damaged maternal tissues must be exposed to this infection.

Another factor may be added: the presence of other organisms that affect the virulence of *Cl. welchii*. Lash[8] reports that the pathogenicity can be considerably increased if the organism is growing in the presence of *Streptococcus haemolyticus*. As this has been confirmed by Falls,[2] we must be a little more guarded as to prognosis if the flora of the birth tract in a case of gas-gangrene infection also contains *Str. haemolyticus*.

CASE REPORT

D. M. (No. 38330), aged 19, was a primiparous white woman whose last menstrual period began December 22, 1938, and whose expected date of confinement was September 29, 1939. She entered the hospital June 28, with

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a history of irregular, cramp-like pains of 15 hours' duration; the membranes had ruptured 10 hours previously. The first trimester of pregnancy had been uneventful. The patient had noticed a sudden gush of blood not associated with any pain at about the end of the 3rd month. She had continued spotting for a few days, after which the bleeding ceased.

Physical examination revealed a well-developed and nourished white woman in labor. The heart rate was 80, regular and of good quality. A harsh, blowing systolic murmur was heard over the pulmonic area. The blood pressure was 118/70. The lungs were resonant throughout. The uterus was enlarged to 22 cm. above the symphysis, and the fetal heart could be heard in the midline, with a beat of 136, regular and of good quality. The presenting parts could not be identified abdominally. Rectal examination revealed the cervix to be effaced but not dilated and the vertex presenting. The temperature was 98.6°F., the pulse 80, and the respirations 20. The diagnoses were pregnancy, 24 weeks, and inevitable abortion.

The labor pains gradually diminished but did not cease. The fetal heart weakened. The following day the temperature rose to 100.6°F. The intrapartum course was uneventful until June 30, when the labor pains increased to every 2 or 3 minutes. The cervix admitted 1 finger, and no fetal heart could be heard. The membranes had been ruptured for 52 hours, and the vaginal discharge, which had previously been clear, turned yellow and cloudy, later becoming green and foul. The temperature gradually rose to 101.6°F., the pulse to 116, and the respirations to 26. The patient was taken to the delivery room at 10 p.m. with the caput showing, and delivered spontaneously a stillborn girl with obvious subcutaneous crepitation all over the body. No maceration was noted, but the skin showed several large, reddish-blue areas. Cervical cultures were taken, and these, together with fetus and placenta, were sent to the laboratory, where smears were made from an incision in the muscles of the back of the fetus, which had a "cooked-meat" appearance. Microscopical examination revealed large gram-positive bacilli. The placenta showed two areas at the periphery, 2 by 3 cm. in diameter, which were fibrotic and grayish white. The patient had a chill 1 hour following delivery, and blood was withdrawn 45 minutes later for aerobic and anaerobic cultures.

The anaerobic blood culture and cervical culture revealed marked gas formation after 10 hours' growth. The organisms were large gram-positive, non-motile bacilli (Fig. 1). Rabbits injected intravenously with organisms from the blood and cervical anaerobic cultures and killed in 10 minutes were blown up with gas after 6 hours' incubation. A guinea pig was injected with the organism cultured from the patient's blood. This pig died within 23 hours with evidence of gas in its tissues, from which pure cultures of large gram-positive bacilli were recovered. A second pig was injected with the identical amount of culture and at the same time as the first pig, but also received simultaneously a dose of polyvalent gas-gangrene antitoxin. This pig was alive and well in 24 hours and remained so. Since *Cl. welchii* is the only organism of the pathogenic group of gram-positive spore-bearing bacilli that is nonmotile, and since it was obvious that the organism had killed the first guinea pig, we believe that this patient had a *Cl. welchii* septicemia. However, further bacteriological studies were carried out, with the following results: dextrose, lactose and saccharose were fermented with the formation of acid and gas; salicin was not fermented; there was no liquefaction of coagulated blood serum; and gelatin was liquefied. Cultures of the organisms from the patient's blood stream and from the guinea pig in litmus milk showed stormy fermentation. All the reactions were typical and conclusive proof of the presence of *Cl. welchii*. Blood cultures taken 24 hours later revealed no growth. Anaerobic cervical cultures taken every other day to July 8 yielded *Cl. welchii*. The next three cultures were negative.

Immediately following delivery a prophylactic dose (5500 units) of combined tetanus and gas-bacillus antitoxin and 4 gm. of sulfanilamide were given. One gram of sulfanilamide and 1 gm. of soda bicarbonate were ordered every 4 hours. One hour later the patient had a chill, the temperature rising to 104.0°F., and the pulse to 140, following which her condition seemed fairly good. A therapeutic dose (23,700 units) of polyvalent gas-bacillus antitoxin was given intravenously 3 hours after the first dose. A third and last injection (23,700 units) of antitoxin was administered 9 hours after the initial dose.

The sulfanilamide dose per day was raised in 24 hours to 6 gm. and continued from July 1 to July 8; it was then diminished to 2 gm. for 2 days and was stopped. The

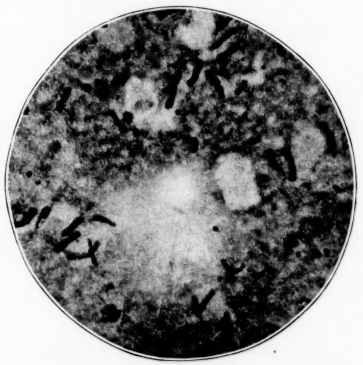

FIGURE 1. *Smear from Anaerobic Culture of the Patient's Blood Showing Heavy Growth of* Cl. welchii.

blood sulfanilamide was between 8 and 9 mg. per 100 cc. until the dose was diminished, when it fell to about 5 mg. During the treatment with sulfanilamide, the patient developed a cyanosis. No evidence of jaundice or of hematuria was ever noted. The red-cell count varied between 4,400,000 and 3,575,000 and the hemoglobin from 88 to 70 per cent during the course of drug treatment. The white-cell count the day after delivery was 25,000, subsequently falling to 18,800.

The postpartum course was uneventful, except for an afternoon temperature rise to 99.5 or 101.0°F. for approximately two weeks. The patient never appeared toxic or felt ill. The uterus involuted properly. She was discharged on July 16, to return in 2 weeks for a checkup, at which time a cervical culture revealed suspiciously large gram-positive bacilli, but anaerobic culture failed to yield *Cl. welchii*.

The sequence of events relative to fetal and maternal infection in this case is of interest. It is

probable that organisms already present in the vagina ascended to the uterus or were carried there during intercourse, douching, bathing or frequent rectal examinations. Did the organisms go from the uterine cavity into the fetus with subsequent production of gas gangrene, or did they

FIGURE 2. *A Section of the Placenta Showing* Cl. welchii *in the Intervillous Spaces.*

invade the placenta and thence the fetal circulation? Granting the possibility of the first sequence of events, we think the latter more probable.

The placenta revealed several areas near the

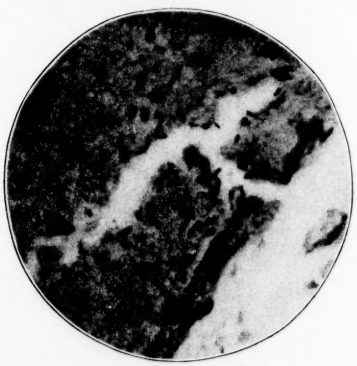

FIGURE 3. *A Section of the Fetal Kidney Showing* Cl. welchii *in the Lumen of a Small Artery.*
A *indicates the wall of the artery.*

periphery that were white and firm. Specially stained sections of these areas revealed the presence of *Cl. welchii* in the intervillous spaces (Fig. 2). The organisms present in the uterine cavity probably wandered in, invaded the dead tissue, grew and penetrated the placenta and thence the general fetal circulation (Fig. 3), with subsequent death of the fetus. The fetal heart sounds were not obtained six hours before delivery, long enough for the classic picture of gas gangrene to develop before extrusion of the fetus.

If invasion was through the placenta with subsequent fetal death, it is reasonable to assume that the mother was infected at the same time, but evidence of severe infection did not develop until two hours after delivery and eight hours after the fetal death. The organisms present in great numbers in the infected endometrial cavity probably invaded the blood clots in the sinuses immediately after delivery, and from there found their way into the maternal blood stream. The mother had no chills prior to delivery, nor did her temperature reach its peak until she had the chill two hours post partum. This sequence of events would seem to suggest that spread of the infection was from the uterine cavity into the fetus ante partum and from the uterine cavity into the maternal circulation post partum.

The treatment of *Cl. welchii* infection in general has seen a change during the last two decades from entire reliance on radical surgery to a more conservative form of therapy, with improved results. To surgery has been added serotherapy, at one time an adjuvant, but now on an equal status. Both have recently been complemented by a new agent, sulfanilamide.

Since most obstetric infections are intrauterine, surgery has always represented a hazardous and limited method of therapy. Obstetricians were forced to use conservative methods. Treatment with serum has had fair results; sulfanilamide now promises better ones. Bates,[9] reviewing the cases of gas gangrene in a large surgical series, from 1926 to 1932, observed that the mortality was 50 per cent, equal to that of the World War period. In this series, the use of serum received but slight attention. Eliason, Erb and Gilbert,[10] reviewing the literature from 1930 to 1936, give the following figures: of 224 patients treated with serum, 56 died, a mortality of 25 per cent; and of 125 patients not treated with serum, 62 died, a mortality of 49 per cent. Millar's[11] statistics also showed a fall in mortality from 43 to 38 per cent following the use of serum. These figures indicate that serum has appreciably lowered the mortality.

Bohlman[12] reported dramatic results in a case of *Cl. welchii* infection from the use of sulfanilamide. The patient had received a prophylactic dose of gas-bacillus antitoxin, but later developed gas gangrene in the lower extremities, for which sulfanilamide was given. It seems necessary to

assume some secondary therapeutic activity of the drug, besides the direct action, because Spray[13] showed in vitro that *Cl. welchii* is scarcely affected by any concentration approaching that tolerated in man.

This patient was treated energetically with both serum and sulfanilamide. Prostration, high fever, abdominal pains and vomiting were absent, although cyanosis was present. Since she received a large amount of sulfanilamide, it is hard to say whether part of the early cyanosis was caused by the infection or by the drug. She never appeared or felt sick during the entire stay in the hospital.

Summary and Conclusions

Clostridium welchii is an organism that will not cause damage unless the conditions are suitable. Once growth starts, the disease is not self-limiting. As the toxins are liberated and more tissue is devitalized, the infection becomes greater. The uterus is a perfect incubator, the dead fetus an excellent medium. Since there is no way of telling whether the dead fetus is infected, one is forced to await the outcome of a delivery before making a diagnosis.

Surgery has no definite place in the therapy of obstetric gas-gangrene infection, because the uterus is not properly situated for surgical attack. Obstetricians are thus limited to conservatism. Antitoxin has proved its worth to some extent. Sulfanilamide seems also to have value. The combination of both appears to be the ideal method of therapy, the drug producing bacteriostasis, and the antitoxin, neutralization of the toxin.

Although each form of therapy has been shown to be curative, it cannot be proved which exerted the greater effect in this case, because both forms were given at the same time and were continued. This case clearly showed that the desired effect can be obtained by combined therapy, because the patient did not develop any of the most distressing of the characteristic symptoms of *Cl. welchii* infection. We believe that this form of therapy will do much toward lowering morbidity as well as mortality.

References

1. Schottmüller, H.: Zur Pathogenese des septischen Abortes. *München. med. Wchnschr.* **57**:1817-1819, 1910.
2. Falls, F. H.: Endometritis and physometra due to Welch bacillus. *Am. J. Obst. & Gynec.* **25**:280-288, 1933.
3. Bysshe, S. M.: The significance of *Clostridium welchii* in the genital tract of pregnant and puerperal women. *Am. J. Obst. & Gynec.* **35**:995-999, 1938.
4. Peckham, C. H.: Statistical studies on puerperal infection. *Am. J. Obst. & Gynec.* **31**:435-443, 582-597 and 996-1003, 1936.
5. De Kruif, P. H.; Adams, T. W., and Ireland, P. M.: The toxin of Bacillus welchii. I. Toxin production by various strains. *J. Infect. Dis.* **21**:580-587, 1917.
6. De Kruif, P. H., and Bollman, J. L.: The toxin of Bacillus welchii. II. The mechanism of infection with B. welchii. *J. Infect. Dis.* **21**:588-599, 1917.
7. Wrigley, A. J.: Puerperal infection by pathogenic anaerobic bacteria. *Proc. Roy. Soc. Med.* **23**:1645-1654, 1930.
8. Lash, A. F.: Puerperal sepsis: B. Welchii, fatal types. *Am. J. Obst. & Gynec.* **25**:288-299, 1933.
9. Bates, M. T.: Gas gangrene; a review of thirty-two cases, with special reference to the use of serum, both prophylactic and therapeutic. *Ann. Surg.* **105**:257-264, 1937.
10. Eliason, E. L.; Erb, W. H., and Gilbert, P. D.: The Clostridium welchii and associated organisms; a review and report of 43 new cases. *Surg., Gynec. & Obst.* **64**:1005-1014, 1937.
11. Millar, W. M.: Gas gangrene in civil life. *Surg., Gynec. & Obst.* **64**:232-238, 1932.
12. Bohlman, H. R.: Gas gangrene treated with sulfanilamide; report of three cases. *J. A. M. A.* **109**:254-256, 1937.
13. Spray, R. S.: Bacteriostatic action of Prontosil Soluble, sulfanilamide, and disulfanilamide on sporulating anaerobes commonly casually associated with gaseous gangrene. *J. Lab. & Clin. Med.* **23**:609-614, 1938.

HYPERINSULINISM (HYPOGLYCEMIA)*

Report of a Case

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HYPERINSULINISM, the antithesis of diabetes mellitus (hypoinsulinism), may be defined, according to Harris,[1] as a disease of the pancreas resulting from the spontaneous hypersecretion of insulin by the islets of Langerhans. It is characterized clinically by hypoglycemia, with the characteristic symptoms, namely hunger, weakness, nervousness, sweating, tremors and mental lapses. Unconsciousness and convulsions may occur in severe cases.

The various factors concerned in the maintenance of the blood-sugar level are shown diagrammatically in Figure 1.

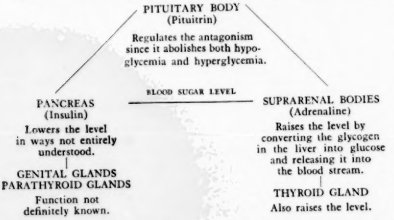
PITUITARY BODY
(Pituitrin)
Regulates the antagonism since it abolishes both hypoglycemia and hyperglycemia.
BLOOD SUGAR LEVEL
PANCREAS
(Insulin)
Lowers the level in ways not entirely understood.
GENITAL GLANDS
PARATHYROID GLANDS
Function not definitely known.
SUPRARENAL BODIES
(Adrenaline)
Raises the level by converting the glycogen in the liver into glucose and releasing it into the blood stream.
THYROID GLAND
Also raises the level.

FIGURE 1. *Factors Concerned in the Maintenance of the Blood-Sugar Level.*

The first recognized case of hyperinsulinism was recorded in March, 1923, by Harris[2] at Birmingham, Alabama. Since this condition is the antithesis of diabetes, the term "hyperinsulinism" was coined at that time. Since then cases have been reported from many different parts of the world. These cases have been classified as mild, moderately severe and severe.

The following report concerns a case of the severe type.

CASE REPORT

The patient, a 27-year-old white, married woman, entered the hospital on April 22, 1939, in a semicomatose condition, in which she had been for 8 hours. She had had a comatose spell in December, 1938, which lasted for 4 hours. One week previous to admission she had had a spell which lasted 10 hours. On both these occasions she was in a profound coma and did not respond to commands or external stimulation. The coma that resulted in hospitalization was said to have started about 6 a.m. The patient remained in a deep coma until 5:30 p.m., when she began to respond to commands and questioning; however, her responses were limited to the answer of her name when asked. She had no aura or fit, no relaxation of the bladder or bowels, no fever or chills, no nausea or vomiting. In later questioning the patient's husband recalled that at 8:30 a.m. she screamed and tried to get out of bed.

The past history revealed that the patient had suffered from frequent frontal and temporal headaches but no visual disturbances. She had had no convulsive seizures, and there was no history of head injury. She had had frequent attacks of epistaxis. No medication was taken by the patient before admission.

Physical examination was essentially negative, except for tachycardia and a rotary nystagmus, which gradually subsided. The extremities were flaccid but showed no paralysis. The reflexes were normal. Negative findings were reported in the urinalysis and in the x-ray film of the skull; the blood picture was normal. The blood sugar was 33 mg. per 100 cc., and the spinal-fluid sugar 18 mg.

A spinal puncture was done; the patient aroused momentarily, but relapsed into coma. Fifty per cent glucose in normal saline solution was given intravenously; this brought the patient out of the coma almost immediately. She was put on a diet consisting of 90 gm. of carbohydrates, 60 gm. of protein and 250 gm. of fat, divided into seven daily feedings. The patient was thin and slightly underweight, hence the high-fat content was thought necessary. Diet alone was not sufficient to keep her free from symptoms, and consequently medication in the form of Tablets Mixed Gland (Burroughs, Wellcome and Company) was prescribed.

Since leaving the hospital the patient has gained 14 pounds in weight. She has had no further attacks and has been able to perform the ordinary household duties. Blood-sugar tests on three different occasions have revealed concentrations of about 70 mg. per 100 cc. Two carious teeth and bridgework were removed as a possible focus of infection. She was last examined on January 14, 1940.

The symptoms in mild cases of hyperinsulinism are excessive hunger, weakness, nervousness, anxiety or irritability one or two hours before meals. These symptoms are relieved by eating. There may also be present perspiration, trembling, flushed face and tachycardia. Vertigo and palpitation have also been noted. In such cases the fasting blood sugar ranges between 60 and 70 mg. per 100 cc. In moderately severe cases the same symptoms may be present, but in the exaggerated form. The fasting sugar level usually ranges from 50 to 60 mg. per 100 cc. The severe cases are characterized by attacks of unconsciousness, with or without convulsions. The blood-sugar levels are very low, findings of 20 mg. per 100 cc. having been reported. In cases presenting suspicious symptoms, routine blood-sugar tests are necessary in order to determine whether hypoglycemia exists.

In mild cases the taking of food between meals and late at night is usually sufficient to control the

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symptoms. The dietetic treatment of moderately severe cases consists in the use of a diet low in carbohydrate, high in fat and normal in protein and frequent feedings.[3] This case of the severe type was treated with diet and gland therapy with marked improvement. There is an advantage in using low-percentage fruits and vegetables, since their slow digestion yields only small quantities of glucose at a time, by which process the minimum stimulation of insulin is brought about. Fats, in the form of milk and cream, given with and between meals, are believed to delay assimilation of the carbohydrates by allowing the stomach to empty slowly.[4] Mixed gland therapy is recommended when the attacks cannot be controlled by diet.[5] Operation on the pancreas is justified in cases in which there is a constant uncontrollable tendency for the blood-sugar level to fall below 50 mg. per 100 cc., thus preventing the patient from earning his living.[6]

To bring a patient out of an attack when he cannot co-operate by swallowing sugar syrup or sweetened orange juice, intravenous injections of glucose must be given. Adrenalin, pituitary extract and thyroid substance have also been used.

The prognosis is usually favorable since in the majority of cases the state is purely functional, with no organic lesion in the pancreas or other glands of internal secretion.

Summary

A case of the severe type of hyperinsulinism is presented and briefly discussed.

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References

1. Harris, S.: Hyperinsulinism, definite disease entity: etiology, pathology, symptoms, diagnosis, prognosis and treatment of spontaneous insulinogenic hypoglycemia (hyperinsulinism). *J. A. M. A.* **101**:1958-1965, 1933.
2. *Idem:* Hyperinsulinism and dysinsulinism. *J. A. M. A.* **83**:729-733, 1924.
3. Piersol's *Cyclopedia of Medicine.* 1063 pp. Philadelphia: F. A. Davis Co., 1936. Pp. 184-195.
4. Beckman, H.: *Treatment in General Practice.* Second edition. 889 pp. Philadelphia and London: W. B. Saunders Co., 1934.
5. Goldzieher, M. A.: Chronic hypoglycemia. *Endocrinology* **20**:86-92, 1936.
6. Judd, E. S.; Allan, F. N., and Rynearson, E. H.: Hyperinsulinism: its surgical treatment. *J. A. M. A.* **101**:99-102, 1933.

REPORT ON MEDICAL PROGRESS

CHILDREN'S SURGERY

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BOSTON

Appendicitis

APPENDICITIS continues to claim consideration, since it remains a factor of major importance in childhood mortality. Better nutritional standards and more effective public-health measures have resulted in a lowered child mortality rate, so that more children are saved from other diseases to suffer from, and all too frequently to die of, appendicitis. The annual number of child deaths from appendicitis has declined but little and the child population appears, temporarily at least, to be stabilized. The general death rate in Massachusetts per 10,000 children under ten years of age was 669 in 1920, 324 in 1930 and 180 in 1936, but the rate for children with appendicitis was 8.2 per cent in 1920, 15.9 per cent in 1930 and 10.6 per cent in 1936.‡ Only pneumonia and accidents exceed appendicitis as a cause of death in this age group.

Unfortunately, the idea remains fixed in the public mind that the young need not be suspected of appendicitis and, more unfortunately, there is reason to suppose that some physicians fail to consider such a diagnosis early in the course of an attack.

Certain facts are established. Appendicitis occurs in the young with reasonable frequency, and is a killing disease if not recognized and treated promptly. There is no nonsurgical method of treatment of merit. Operation before peritoneal infection is present is absolutely curative, with essentially no surgical risk. When properly managed the young are excellent anesthetic and surgical risks, but they must be well managed.

Considering these facts, control of morbidity and mortality can be reduced to three elementals: first, the public must realize that a physician should be called promptly whenever there is a complaint of abdominal pain; second, physicians must become "appendix-conscious" and really examine the child patient; and third, appendectomy must be performed expeditiously if a diagnosis is established, and such operation should be considered seriously if appendicitis cannot be excluded from

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‡These statistics represent calculations by Dr. H. W. Hudson, Jr., from material submitted by the Massachusetts Department of Public Health, and refer to conditions in Massachusetts only.

diagnosis. If these conditions were fulfilled there would be no appendicitis problem. Until a level of education is reached which attains these three elementals, both long periods of morbidity and deaths will result from peritonitis of appendiceal origin. It is my considered opinion that discussion of treatment of the desperately ill patient should be confined to surgical meetings and surgical literature. I believe that open discussion of methods which are still matters of surgical opinion has resulted in harm, in that it may have given rise to the entirely erroneous idea that there is both a medical and a surgical method of managing appendicitis. *There is no medical treatment.* The questions of delayed operation with Ochsnerization (with its modifications), drainage versus no drainage, enterostomies of various types, serotherapy, chemotherapy, the use of coli-bactrogen, types of incision used to approach an appendix, and the time at which to approach it, and the use of drugs to maintain intestinal tone or stimulate peristalsis will not be discussed here.

Decompression of the intestine by means of Wangensteen's[1] technic, lessening of distention by the use of an atmosphere of high oxygen tension, as recommended by Fine, Hermanson and Frehling,[2] the control of hydration, the maintenance of blood-electrolyte levels, the prevention of ketosis by parenteral fluid administration and the use of blood transfusion for low serum-protein levels are all advances of proved merit in the control of the desperately ill.

Real progress will be made when children are referred for surgery earlier in the course of their disease. In this connection the lowering of mortality in the Children's Hospital series of cases of proved acute appendicitis with and without complications is encouraging. For the period 1929–1938 the death rate was 3.06 per cent, for 1929–1933 it was 3.6 per cent, for 1933–1938 it was 2.3 per cent, and for 1938 and 1939 it was 2.2 per cent.[3] Although improved methods play a leading role in this reduction, the fact that fewer patients presented peritoneal complications was also significant. This, we believe, represents progress in the control of appendicitis mortality.

Empyema

The treatment of acute empyema, especially in children, has received much discussion since the war. The three forms of treatment — repeated aspiration, intercostal closed drainage and open drainage, with or without rib resection — have each had their strong proponents and opponents. It is becoming more widely appreciated, however, that each of these methods has its usefulness, its indications and its contraindications. It is fundamental to realize that each patient must have that form of treatment that is best suited to the etiologic organism, the stage of the disease and the age of the patient. The improvement in the results during the last five years at the Children's Hospital[4] was effected largely because no routine form of treatment was used. One, two or all three forms of treatment have been used as the individual case warranted.

Acute empyema should never be regarded as a surgical emergency but rather as a complication of an acute primary disease. Diagnostic aspiration is important in all cases, and methods of drainage should be based on the bacteriological findings as well as on the stage of the disease and the age of the patient. During the pneumonic stage treatment should be instituted only when necessary in order to relieve the mechanical embarrassment of the heart and lungs, and then only by repeated aspiration or occasionally by closed drainage. Open drainage should never be done in the pneumonic stage. In properly selected cases, however, primary rib resection is a rapid and efficient method of treatment, and it is also useful as a secondary procedure when intercostal drainage has proved inadequate. Local anesthesia for aspiration and intercostal drainage, and nitrous oxide and oxygen for open drainage, are favored. Scoliosis need not be feared if the cavity is well drained and the lung re-expanded. By following these principles the mortality has been reduced in the last five years to 2 per cent in 137 cases. The mortality in patients under two years of age was reduced to 4 per cent in 46 cases.

Chronic Pulmonary Suppuration

Chronic suppurative lesions of the lungs in children can be treated successfully by radical lobectomy or pneumonectomy, and these radical procedures should not be withheld on account of the age of the patient. Although the causative agent in many cases of pulmonary chronic suppuration is obscure, prevention is of course far better than treatment after suppuration has occurred. Particularly in this age group the possible presence of a foreign body must always be considered and ruled out in any case of infection of the lung that does not respond to the usual therapy. The presence of an atelectatic lobe in recurrent pneumonia must also be considered as an underlying cause of chronic suppurative disease in the lung. In many cases, chronic lung suppuration that follows acute empyema can probably be avoided by adequate treatment of the empyema during its acute stages. There remain other cases for which no definite etiology has as yet

been found. These cases need careful bacteriological study and the closest observation, including repeated x-ray photographs after injection of Lipiodol. If, after a varying period of weeks, the process shows no signs of improvement, radical removal of the diseased portions of the lung must be considered. With too long a delay the process may go on to gangrene and so preclude successful radical removal. It is difficult as yet to assign any absolute time limit at which radical treatment should be instituted.

At the Children's Hospital there have been 14 lobectomies performed for chronic lung suppuration, with no deaths. There have been 6 total pneumonectomies, with 2 deaths. One of these deaths might have been avoided had radical surgery been done at an earlier stage of the disease.

Duplication of the Alimentary Tract

Duplication of the alimentary tract is a term which has been used to describe a condition which has heretofore received a variety of titles, none of which are both accurate and inclusive.

Pathology

Duplications of the alimentary tract are hollow structures which possess two muscular coats and are lined by epithelium similar to that found in various segments of the gastrointestinal tract. These lesions are almost always contiguous to some portion of the alimentary tube. The type of epithelium lining the duplication does not necessarily correspond to that part of the alimentary tract to which the structure is attached. The cystic structure may or may not communicate with the adjacent intestinal lumen.

An important finding is the histological fact that the muscular coats of the duplication are intimately associated with or are an integral part of the muscularis of the alimentary tract.

The contents of the duplication vary with the type of epithelium lining the structure, with the presence or absence of a communication of the adjacent intestine and with the presence or absence of necrosis of the duplication wall. If there is a communication with the bowel, the duplication contents naturally are similar to those of the adjacent bowel. If there is no communication, the contents usually contain a clear, colorless fluid of mucoid consistence.

Clinical Findings

This condition is usually observed in children. The symptoms may be grouped under three headings: obstruction of the alimentary tract by regional external pressure, pain produced by distention of the cystic structure and hemorrhage because of interference with the intestinal blood supply, leading to sloughing of the intestinal mucosa.

Duplications may occur at any point from the mouth to the rectum, and the symptoms, of course, vary with the location of the condition. In a lesion appearing at the base of the tongue, difficulty in swallowing was the outstanding symptom in this series. With the duplications in the mediastinum, difficulty in swallowing and interference with expansion of the lung leading to dyspnea were the prominent symptoms. In a duplication of the stomach, the symptom was that of epigastric fullness and pain, produced by tenseness in the mass. Most of the cysts of the duodenum, jejunum and ileum brought early signs of partial intestinal obstruction, characterized by colicky pain, vomiting, increased peristalsis and finally signs related to dehydration. In a duplication of the terminal ileum, the complaints were related to severe painless hemorrhage from the lower intestinal tract caused by ulceration and sloughing of the ileal mucosa. In one case the duplication of the ileum was the advancing point of an intussusception, and gave the usual symptoms of that condition. The duplication of the rectum caused early constipation and abdominal distention.

By physical examination these masses can usually be felt and a correct diagnosis is often suggested. The tumors were elastic, usually nontender and well rounded, and except for the duodenal lesion, were quite freely movable within the abdominal cavity. Intestinal duplications all showed signs of partial intestinal obstruction, such as visible peristalsis, localized abdominal distention and increased audible peristaltic activity. The cyst of the rectum could be easily palpated by rectal examination, and was sufficiently large so that the examining finger could not be pushed beyond the compressed point.

Treatment

The structure of these lesions is important in relation to operative procedures. First, the cyst and the intestine have a common wall and the two cannot be dissected apart with safety. Second, an attempt to remove the cystic structure locally may interfere with the blood supply of the intestine and cause necrosis.

The thoracic lesions may present great difficulty, particularly in the very young. Freeing the cystic structure from the lung is comparatively simple, but when one attempts to dissect it from the esophagus there is danger of entering the esophageal lumen, and the possibility of a fatal mediastinitis or an empyema or an esophageopleural fistula is great. As a result of my experience, I believe that these cases are better treated

by marsupialization of the cyst through the posterior thoracic wall, combined with subsequent destruction of the cyst lining by the use of sclerosing fluid.

The duplications of the intestine from the duodenum down require excision of the cystic structure with the adjacent intestine and an anastomosis. In a small infant a lateral anastomosis is the operation of choice on account of the small lumen of the intestine.

It is a distinct advance to recognize this condition as a distinct clinical entity, and to practice complete excision with the adjacent portion of the alimentary tract when possible. Otherwise, marsupialization and destruction of the mucous membrane lining are recommended. In recent years at the Children's Hospital 18 cases have been observed, 14 of which were treated on these principles, and in 11 of these the patients have recovered with satisfactory results.

Diaphragmatic Hernia in Infancy

Little attention has been paid in the literature to diaphragmatic hernia in newly born babies, and a further study of this condition is warranted because the operative treatment promises such excellent results. Except for small diaphragmatic hernias occurring at the esophageal hiatus, most patients are apt to die in the first weeks or months of life. It is probably a fair estimate to say that 75 per cent of these individuals will die if no therapeutic measures are instituted. Isolated reports indicate that surgical treatment can be undertaken, is well tolerated and gives promise of a lasting cure. A review of the literature shows that at least 17 infants under one year of age have been successfully operated on, and at the Children's Hospital an additional 6 cases in this age group have been thus successfully treated.

The diagnosis is not difficult to make. In any newly born infant or young child with dyspnea, coughing, cyanosis or vomiting, diaphragmatic hernia must be considered. On physical examination the breath sounds are greatly diminished or absent over the affected side; the percussion note on the affected side may be tympanitic if gas-filled loops of intestine are present, or dull if the liver or fluid-filled loops of intestine are in the chest. With the massive displacement of intestine upward into the thorax, the abdomen is apt to be flat or even scaphoid.

The most important examination in establishing the diagnosis is that consisting of roentgenological study. Films of the thorax and abdomen without the use of contrast media usually give all the information that is necessary. The pleural cavity will be partially or completely filled with loops of intestine, colon, stomach or possibly portions of the liver. The lung on this side is replaced and collapsed. The mediastinum and heart are pushed to the opposite side and the opposite lung is partially compressed. Ingested barium will give additional information regarding the position of the stomach and intestines, and a barium-enema study will demonstrate the position of the colon. These findings are of interest but have little practical value, and the danger of producing obstruction with inspissated barium or the danger of aspirating this material is relatively high. Therefore, such examinations should usually be omitted.

For the operative treatment, positive-pressure anesthesia should always be employed, and at the present time cyclopropane is the anesthetic of choice. Babies who are cyanotic and have great respiratory distress take this anesthetic particularly well. It is probably best to paralyze the diaphragm by exposing the phrenic nerve in the neck and crushing it. Undoubtedly the best operative approach is by way of the abdominal cavity. This gives adequate exposure of the diaphragmatic defect. After the abdominal viscera have been withdrawn from the pleural cavity, the diaphragm is repaired with interrupted sutures of silk. The most difficult part of the operation is the closure of the abdominal wound, because the abdominal cavity is too small to accommodate the viscera which have to be placed in it.

Experience with surgical treatment in these cases demonstrates that it is a fallacy to delay operation in the hope of improving the general condition of the baby. Operation should be performed when the diagnosis is made. It is preferable to perform the operative repair in the first forty-eight hours of life, because in this period the intestines will not have distended and can be more easily replaced in the abdominal cavity.

Of 8 patients successfully operated on at the Children's Hospital, 6 were in the first year of life, and their ages were forty hours, eleven days, three weeks, four weeks, six weeks and nine months. These results indicate that the condition of congenital diaphragmatic hernia is amenable to surgical therapy, and that babies with this condition should be so treated.

Neurosurgery

There has continued to be an apparent increase in frequency of subdural hematomas in infancy. I believe that this is entirely due to the effort which is being made to investigate thoroughly a larger number of patients with unexplained symptoms and signs. The fact that mechanical meas-

ures, namely tapping or exploratory burr holes, are necessary becomes increasingly clear as data on these cases accumulate. I am correspondingly less impressed by the lack of history of trauma in these patients. Although parents are carefully questioned on this point, young patients are continually seen with extensive fractures but no history of injury. These fractures have for the most part been seen in otherwise normal bones, and are presumably not due primarily to a deficiency state.

A preliminary survey of the intracranial tumors verified in the Children's Hospital since 1930 shows an interesting pathological distribution. The relative frequency of the various types of tumors in this series does not correspond to those previously reported by others, this difference being of significance chiefly because of the current impression that medulloblastoma is the commonest intracranial tumor of childhood. This impression has, in fact, been advanced as an argument in favor of radiation therapy without exploration, decompression and biopsy. In the series there were 32 astrocytomas and 19 medulloblastomas, a sufficient preponderance of the surgically favorable type to make the supposed high frequency of medulloblastoma an entirely incorrect basis for such therapy. In addition, an analysis of the histories shows that it is frequently quite impossible to make an accurate preoperative pathological diagnosis, preoperative radiation therefore resulting in a very serious loss of time in the less invasive tumors.

The other 35 tumors in the series showed a wide range of cellular structure, from entirely benign dermoid cysts to very rapidly growing invasive tumors, such as glioblastoma multiforme. There were 7 craniopharyngiomas, 1 of which it was possible to remove in its entirety without residual damage. In the other craniopharyngiomas evacuation of the cyst, with piecemeal and presumably incomplete removal of the wall, had to suffice, but the results even in these cases have been very encouraging. It is obviously essential that these patients receive whatever treatment is possible at an early date before optic atrophy has progressed too far.

It may be worth while emphasizing the fact that children with signs of increased pressure, such as headache, vomiting, papilledema and so forth, or with any disturbance of motor function, except when it is known to be due to a fixed lesion, should receive a complete neurological study, and if there is any doubt whatever they should be suspected of having a brain tumor and examined at frequent intervals with that possibility in mind. There is ample proof that many brain tumors of childhood are susceptible of surgical treatment with little or no residual damage if operation is done early enough. In the presence of an operable tumor, the removal of which offers a good prognosis, it is therefore extremely important to avoid preliminary trial x-ray therapy or prolonged observation which may leave permanent blindness or motor dysfunction.

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REFERENCES

1. Wangensteen, O. H.: Early diagnosis of acute intestinal obstruction with comments on pathology and treatment, with report of successful decompression of three cases of mechanical bowel obstruction by nasal catheter suction siphonage. *West. J. Surg.* **40**:1-17, 1932.
2. Fine, J.; Hermanson, L., and Frehling, S.: Further clinical experiences with ninety-five per cent oxygen for the absorption of air from the body tissues. *Ann. Surg.* **107**:1-13, 1938.
3. Hudson, H. W., Jr., and Chamberlain, J. W.: Acute appendicitis in childhood; a statistical study of 848 cases from the Children's Hospital, Boston. *J. Pediat.* **15**:408-425, 1939. Also, unpublished data.
4. Lanman, T. H., and Heyl, H. L.: Empyema in children. *New Eng. J. Med.* **221**:1003-1009, 1939.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26091

PRESENTATION OF CASE

A fifty-six-year-old man was admitted to the hospital complaining of painless hematuria.

The patient had enjoyed perfect health until one week before admission when for the first time he passed a large amount of bright-red blood in his urine. Following this he noticed a sharp non-radiating pain in the right flank, which lasted some twenty minutes and disappeared gradually without residual discomfort. He continued to pass blood in decreasing amounts for the next four days. For three days before admission, however, the urine was "dark," but no fresh, bright-red blood was noted. He had experienced no chills, fever, nocturia, frequency, urgency, dysuria or pyuria. He had lost no weight and had noted no other symptoms.

The patient had been in close contact with a brother, who had spent six months of the past year in a local sanatorium because of "weak lungs," and a niece, who had died of tuberculosis eight years before the patient's present illness. The remaining family, marital and past histories were negative.

Physical examination revealed a slender, well-developed man, who lay quietly in bed in no apparent distress. The teeth were carious. Examination of the heart, lungs and abdomen was not remarkable. The genitalia were negative except for the presence of a small, smooth, cystic mass in the globus major of the right epididymis. The rectal examination was negative. The blood pressure was 150 systolic, 80 diastolic.

The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 5,300,000 with 17.7 gm. hemoglobin (photoelectric-cell technic), and a white-cell count of 19,000 with 78 per cent polymorphonuclears. The blood smear was negative; the platelets were normal. The urine was cloudy, amber in color and acid, with a specific gravity of 1.016 and a + albumin test. The sediment contained 40 to 150 red blood cells, 5 to 8 white blood cells and 2 epithelial cells per high-power field. The blood Hinton test was negative. The blood sugar and nonprotein nitrogen determinations were normal. Culture of bladder urine showed a moderate growth of *Staphylococcus aureus* and an abundant growth of nonhemolytic streptococci.

Intravenous pyelograms showed that the kidneys were normal in size, shape and position. There were no visible stones. The intravenous dye appeared promptly and demonstrated normal urinary passages on the left. On the right side there was a sharply defined filling defect occupying the upper major calyx and upper portion of the renal pelvis. The lateral margin of the pelvis in this area showed a slight pressure defect, and there appeared to be slight spreading of the upper and middle calyces. The bladder showed a pressure defect in the region of the prostate. A right retrograde pneumopyelogram confirmed these findings. There was a definite intrapelvic filling defect in the right kidney, which was the same size and shape as that previously demonstrated by the intravenous pyelograms. The margins of this defect were slightly irregular, and it appeared to extend upward along the upper calyx of the kidney. The bladder was not demonstrated.

On the fifth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. J. DELLINGER BARNEY: The causes of hematuria are legion and we cannot go into all of them here. When we speak of painless hematuria we usually mean that there are no particular symptoms associated with it. This patient had right flank pain, and there are many causes, of course, for that. But we have to consider the possibility that this man had a tumor in this kidney, the pain being caused not by the tumor but by the formation and passage of large blood clots. Or, he might have had an acute inflammatory disease of the kidney—I refer to carbuncle or multiple cortical abscesses. Or, he might have had a perinephritic abscess, or an acute hemorrhagic nephritis, in which, as Dr. Holmes and I recall very well, the findings may very strongly suggest those of a renal tumor. The fact that he had lost no weight indicates it was not a long-standing process.

His association with two individuals who apparently had tuberculosis might throw some light on the question, but I do not believe it does in this particular case. With the story we have already heard and contact with these individuals, we have to consider the possibility of tuberculosis of the urinary tract. On the other hand, in my experience, renal tuberculosis does not produce massive hematuria or pain, and there is microscopic hematuria rather than gross.

The fact that the temperature, pulse and respirations were normal indicates there was no acute

inflammatory process in the urinary tract. The lungs were said to be negative but that does not absolutely rule out tuberculosis. It comes rather close to it, however. From the description I should think the mass in the epididymis was probably a spermatocele, which occurs not infrequently, is smooth and cystic, varies in size from that of a pinhead to that of an English walnut, occurs in the globus major, and would probably not be confused with epididymal tuberculosis. This might have been a neoplasm of the testicle or the epididymis, but I believe it was a spermatocele. The fact that the rectal examination was negative indicates that there was no obstructing prostate which was large enough to protrude into the rectum. It also suggests that there was no abscess, carcinoma or tuberculosis of the prostate.

Examination revealed that the blood picture was essentially normal. The rather high white-cell count may have been secondary to hematuria or, in other words, to the loss of blood. The urine apparently had cleared and was no longer grossly bloody, but the fact that it contained red cells indicates residual blood or persistent, although diminished, hemorrhage. We can rule out any serious inflammatory process by the fact that there were very few white cells in the sediment. Apparently there was very little kidney damage, inasmuch as the blood nonprotein nitrogen was normal.

Culture of the bladder urine showed that it did contain bacteria, but we not infrequently culture organisms of one sort or another, even streptococci or staphylococci, without fever and other clinical manifestations of sepsis. One would have to hunt for the possible focus from which these bacteria came.

The fact that the intravenous pyelogram showed the kidneys normal in size, shape and position tends to eliminate certain things, namely kidney tumors such as hypernephroma or adenocarcinoma, which would probably have caused enlargement of the kidney or an irregularity in its contour where the tumor bulged out from the side. In tuberculosis of the kidney one might not get any particular change. In an inflammatory condition, such as a pyelonephritic kidney, one would find a larger kidney than is normally found. A solitary cyst generally indicates its presence by deformity of the normal kidney outline, but we cannot rule it out. The dye was excreted normally and apparently equally by both kidneys, so that the kidney function was good. In other words, the cortical substance of the kidney had not been badly damaged. But on the right side we find a filling defect occupying the upper major calyx and the upper portion of the pelvis. This filling defect was found again in the retrograde pyelogram, as we may see in the x-ray films. Obviously there was something affecting the pelvis and upper major calyx. The filling defect in the bladder in the region of the prostate may have been due to an enlarged lobe of the prostate. We may see very markedly enlarged prostates at the age of fifty-six, but such is not usually the case. The rectal examination is said to have been negative, however, which would be improbable had there been an enlargement of the prostate sufficient to cause a filling defect in the x-ray film. The filling defect might have been due to tumor of the bladder or to a blood clot which was lying in the bladder. There are various possibilities.

May I see the x-ray films?

Dr. George W. Holmes: Apparently we do not have the film that shows the injected pelvis.

Dr. Otto Sahler: There was only an air injection.

Dr. Holmes: I am glad to know this. I thought I was looking at gas in the colon. You can see the deformity described, also in this film the filling defect and the narrowing of the upper calyx. Of course the patient had been bleeding, and you have to consider the possibility of blood as well as that of tumor. Blood clots as a rule do not extend into the upper calyx without involving the lower calyx. The character of the defect itself is not that seen with blood clot, and we have further evidence of a deformity in a film taken on another day. I think we are safe in saying that it does represent a true lesion in the kidney pelvis. The films do not permit me to say positively that the lesion is a tumor.

Dr. Barney: As you can see fairly well, the kidney outline is normal in size, without bumps on its contour such as would be expected with a tumor of the cortical substance. But I am interested in this moth-eaten appearance in the pelvis. It looks, in these air injections, as if there was a tongue-like process hanging down into the pelvis, and the same tongue-like lesion is evidently the dye-filled pelvis subsequent to the intravenous pyelogram. You can see it quite definitely in both films, a fact that clearly demonstrates the value of air injection of the renal pelvis. I am not so much impressed with the filling defect in the region of the prostate. The bladder is moth-eaten and ragged and has the appearance of one that is obstructed and trabeculated. This defect may represent the prostate, a tumor — neoplasm of the bladder — or a blood clot, but I do not believe it is either. I think it is probably prostate plus trabeculation. Although I am always looking out for pitfalls at these conferences, I shall hazard a

guess that this was an intrarenal pelvic tumor of the papillary type, the pain being due to the attempted passage of clots, and that such a tumor probably accounted for the whole story.

DR. TRACY B. MALLORY: Dr. Smith, have you any comment?

DR. GEORGE G. SMITH: I should agree, although I do not believe it is papillary. It looks a bit irregular, but I think it is a little more opaque to radiation than a papillary tumor would be. I believe it was a solid tumor of the kidney pelvis. If it were stone, it would not stick up or interfere with the upper calyx.

CLINICAL DIAGNOSIS

Neoplasm of right kidney?

DR. BARNEY'S DIAGNOSIS

Tumor of right renal pelvis (papillary type).

ANATOMICAL DIAGNOSIS

Papillary carcinoma of right renal pelvis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was explored, and a kidney normal in size and shape was found. A tumor could be felt, however, in the pelvis, and a resection was carried out. The specimen showed a tumor arising in the middle calyx which projected into the pelvis in papillary fashion but also involved a considerably larger portion of the pelvis as a flat sessile tumor. It did not appear to descend down the ureter.

Microscopical examination showed a papillary type of carcinoma with rather more than an average grade of malignancy. It was quite undifferentiated and rapidly growing.

The outcome of the case was tragic, as two days after operation he suddenly developed the symptoms of massive pulmonary embolism and died instantaneously. There was no post mortem, so I cannot tell you what the condition of the bladder and prostate was. In this type of tumor it is of course not uncommon to find involvement of both the homologous ureter and the bladder.

CASE 26092

PRESENTATION OF CASE

A nine-and-a-half-year-old girl was admitted to the Eye and Ear Infirmary with a complaint of a discharging right ear.

About two months before entry the patient developed a sore throat and a right earache. After a few days some discharge appeared from this ear, and after ten days a paracentesis was performed, a purulent discharge continuing until admission. Two days before coming to the hospital postaural swelling appeared and the child was said to be feverish.

The patient had had measles, chicken pox, whooping cough and pneumonia. A tonsillectomy and adenoidectomy were done four years before entry. Two and a half years prior to admission there had been discharge from the right ear, fever and headache; she was admitted to a hospital for a suspected meningitis, but the symptoms subsided in a short time. A year before entry she had had abdominal pain, which was said to be the result of "inflammation of the kidneys."

Physical examination showed a well-developed and nourished girl in no acute discomfort. There was slight injection of the pharynx, and a profuse mucopurulent discharge from the right ear. Slight postaural tenderness was elicited, but there were no signs of meningeal irritation. The remainder of the examination was negative.

The temperature was 101.6°F., the pulse 115, and the respirations 22.

Examination of the urine was negative. The blood showed a white-cell count of 22,000, with 77 per cent polymorphonuclears.

The patient's temperature varied between 100.0 and 103.0°F. during the first six days, and the postaural tenderness persisted. On the seventh day the temperature rose to 105.5°F. and she vomited several times. A right simple mastoidectomy was done and a perisinus abscess was found. Two days postoperatively she had a severe chill lasting for fifteen minutes. A blood culture showed a growth of hemolytic streptococci. A second operation was performed with ligation of the right jugular vein. There was no thrombosis, but a definite phlebitis was present. On the tenth hospital day she showed, for the first time, a positive Kernig sign and a stiff neck; a lumbar puncture was normal. Thereafter she complained of transient severe pain in the right hip, and the temperature remained elevated to 105.0°F. On the fifteenth day there was some bleeding from the neck wound and a third operation for religation of the jugular vein was performed. Two days later the left ear began to discharge yellow pus, and after three days a transfusion was given. Her temperature gradually fell to 100.0°F., but on the twenty-fifth day the eyelids became puffy and the urine smoky. The latter contained a large trace of albumin and many red and white blood cells. During this time the temperature occasionally reached 102.0°F. but remained for the most part near 100.5. The blood pressure was 130

systolic, 75 diastolic, and she began to vomit. Examination of the eyegrounds showed beginning choked disks. There were no signs of meningeal irritation at this time. Vomiting persisted for a week, despite the administration of intravenous glucose.

Ten days after the appearance of the puffy eyelids the blood nonprotein nitrogen was 81 mg. per 100 cc., the serum protein 4.9 gm., and the cholesterol 191 mg. There was beginning pitting edema of the ankles and in the sacral region. Another lumbar puncture done two days later showed an initial pressure of 350 mm. of water, and 15 cc. of "ground glass" fluid was withdrawn. The fluid contained 1700 cells per cubic millimeter, 87 per cent of which were polymorphonuclears. The total protein was 46 mg. per 100 cc., and the sugar 43 mg.

No organisms were seen in the smear.

At the end of thirty-eight days the temperature again rose to 104.0°F., but no further surgery was attempted. Vomiting persisted; there was some frontal headache, and the general condition did not appear to be very good. Subsequent lumbar punctures showed continued cloudy fluid under increased pressure; there appeared stiffness of the neck, bilateral Kernig signs and a Brudzinski sign, and the optic disks were markedly blurred. The urine showed a trace of albumin with 8 to 10 white blood cells per high-power field and a few casts. The white-cell count of the blood, which had ranged between 19,000 and 25,000, rose to 35,000 and then to 50,000. Cultures of the spinal fluid showed hemolytic streptococci on three occasions, and the spinal-fluid sugar dropped to 16 mg. per 100 cc. On the forty-first hospital day she had a generalized convulsion, became comatose and exhibited markedly irregular breathing. She died two days later, on the forty-third hospital day.

Differential Diagnosis

Dr. Theodore H. Ingalls: This patient started off a protracted and fatal illness with an acute otitis media following an upper-respiratory infection. The right drum ruptured spontaneously, was later incised, and continued to drain for two months, making the diagnosis of right mastoiditis presumptive if not certain. It is of merely passing interest that otitis media had occurred two and a half years before entry and that her tonsils and adenoids had been removed long before either infection. Whether "inflammation of the kidneys" a year before entry represented pyelitis, nephritis or simply a lay diagnosis I am unable to say.

She was admitted to the hospital with postaural tenderness, obviously related to mastoiditis on the right. For the following week, during which she was studied and presumably x-rayed for signs of osteomyelitis, her condition remained substantially the same, with discharge persisting from the ear, a fever of 100.0 to 103.0°F. and an elevated white-cell count. Then there occurred a change to which I am inclined to attribute considerable significance. The temperature rose to 105.5°F. and she vomited several times. Since this occurred before operation, and in fact must have been the main consideration leading to operation the same day, it seems likely that it represented a sudden extension of a septic process in the way of a phlebitis of the lateral sinus. In point of fact a definite phlebitis resulting from a perisinus abscess was found, and a hemolytic streptococcus cultured from the blood stream two days later. I am inclined to believe that the phlebitis dated from the first sharp temperature rise and that streptococci could likewise have been recovered from a blood culture taken at that time. Exactly when the patient picked up the streptococcus is difficult to say. I should suppose that it was in the ear and nasopharynx for some time and that the sudden temperature rise marked its invasion into the blood stream. One cannot help speculating as to whether a massive initial dose of sulfanilamide administered immediately after the temperature rise and prior to operation would have changed the end result—it is obvious that this case antedates the sulfanilamide era.

Three days after mastoidectomy, and one day after ligation of the jugular vein, two other changes occurred which are suggestive, although perhaps misleading. A positive Kernig sign and a stiff neck were elicited in the face of a normal lumbar puncture, and "transient severe pain" occurred in the right hip. Since this child had a phlebitis that was feeding bacteria into the blood stream, these symptoms suggest metastases to a joint and to the central nervous system, well-recognized sites of predilection when extension does occur. However, no objective signs were later recorded that suggest involvement of the hip in a septic process, and the transient stiff neck might be related to dural irritation in the neighborhood of the lateral sinus.

From this time on the child maintained a high temperature with signs of continued infection, as revealed by the appearance of a discharging ear on the left, although there was a generally favorable reaction to transfusion, with subsidence of the temperature by lysis to a little over 100.0°F.

Choking of the disks, which then occurred, may reflect an expanding intracranial lesion (abscess) or simply be a result of ligating the jugular vein.

Just eighteen days after the hemolytic streptococcus presumably reached the blood stream, and sixteen days after it had been demonstrated there, the patient developed puffy eyelids and gross hematuria. Although I at first considered pyelonephritis as seriously as glomerulonephritis, the clinical picture of the latter disease is so complete and its time relation — sixteen to eighteen days — to streptococcal invasion so characteristic as to make the latter diagnosis practically compulsory. I find a complicating nephritis in this patient particularly interesting in the light of recent work showing that streptococcal toxin endows homologous (and non-antigenic) kidney proteins with antigenic properties. This explains how a patient such as this might develop circulating antibodies against his own kidney tissue and is one theory as to the etiology of glomerulonephritis. The blood nonprotein nitrogen was definitely elevated, and the serum protein just below the critical level — consistent with the pitting edema present clinically. These figures may have been and probably were influenced by anabolic and starvation processes, since it seems doubtful that an adequate food intake could have been maintained during this illness. Taken in conjunction with the urinary findings they suggest a mild renal insufficiency, which I do not believe constitutes uremia. The blood pressure was only slightly elevated, whether from the intracranial or renal disease I cannot say.

At the end of thirty-eight days the patient developed a terminal meningitis with spinal rigidity and marked choking of the disks. The temperature and white-blood-cell count rose markedly, the spinal-fluid sugar dropped to 16 mg. per 100 cc., and streptococci were cultured on three occasions. I do not know whether this resulted from the extension of a brain abscess into the subarachnoid space — an unusual occurrence — or to direct extension of the septic process in the right mastoid region, which is more likely on the basis of chance.

The facts that some improvement was manifest after transfusion and that the white-blood-cell count was maintained between 25,000 and 50,000 terminally again bring one back to speculate whether sulfanilamide administered when the phlebitis developed might not have proved of decisive therapeutic aid.

DR. HAROLD L. HIGGINS: *Streptococcus haemolyticus* meningitis following a mastoiditis usually occurs by extension extradurally from a perisinus abscess or intrapially from a neighboring metastatic brain abscess. At first the meningeal infection is localized, and the meningitis will frequently subside of itself, if the extrameningeal pus is drained; unfortunately, it was not the case here.

The usual etiology of hemorrhagic nephritis is an acute hemolytic streptococcus infection fourteen to twenty-one days previously and chilling of the body within twenty-four hours; we have no history of chilling in this case. The occurrence of nephritis while the streptococcal infection is still present leads to a more persistent nephritis and a poorer resistance to the bacteria; we observe this here.

CLINICAL DIAGNOSES

Right otitis media, suppurative, acute, with mastoiditis.
Lateral (right) sinus thrombosis.
Acute nephritis.
Meningitis.

DR. INGALLS'S DIAGNOSES

Otitis media: chronic, right ear; acute, left ear.
Osteomyelitis, right mastoid.
Perisinus abscess, right lateral sinus.
Thrombophlebitis, right lateral sinus.
Meningitis, streptococcal.
Brain abscess?
Glomerulonephritis.

ANATOMIC DIAGNOSES

Acute meningitis, hemolytic streptococcus.
Mastoiditis, acute and chronic, right.
Otitis media, acute, left.
Sinus thrombosis, both lateral sinuses, torcular and posterior portion of superior longitudinal sinus.
Nephritis, acute glomerular.
Septicemia, hemolytic streptococcus.
Hydropericardium.
Ascites, slight.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: Dr. Ingalls was quite correct in his surmise that this case antedated the sulfanilamide era. At the present time sulfanilamide would almost certainly have been given a trial and it is quite possible that the outcome would have been different. In fact the most notable difference attributable to chemotherapy in the material which reaches our autopsy table is the marked diminution in the complications of middle ear and mastoid disease.

The autopsy showed a diffuse seropurulent meningitis. Hemolytic streptococci were recovered on culture, and chains of cocci were readily visible microscopically in sections of the meninges. There was no cerebral abscess. Rather extensive granular thrombosis was found involving the pos-

terior half of the superior longitudinal sinus, the torcular and both lateral sinuses extending as far as the jugular foramen on the left side and to the region of the emissary vein on the right. The petrosal and cavernous sinuses were negative. There was still some persisting infection in a few mastoid cells near the posterior portion of the process. The left mastoid was negative, but the left middle ear contained frank pus. The ethmoid and sphenoid cells were negative.

The other important finding was the condition of the kidneys. They were greatly enlarged, weighing 400 gm., as against a cardiac weight of 150 gm. The cortices were something over a centimeter in thickness and appeared very pale, with scattered bright-red petechiae.

On microscopical examination no normal glomeruli could be found. There were marked endothelial proliferation, considerable hemorrhage and fibrin deposit, and occasionally slight crescent formation. From the appearance of the kidneys I should guess that there had been a real uremia in the terminal stages. There was a moderate amount of fluid in the pericardium; this was faintly turbid, but there was no fibrin and a septic pericarditis could be excluded.

The New England
Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
The New Hampshire Medical Society
The Vermont State Medical Society

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States; Canada, $7.04 per year; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

WHAT IS OSTEOPATHY?

This question has been asked on numerous occasions recently in medical literature and the answers have been such that there appears to be a golden opportunity for some medical historian to write in objective fashion an account of the rise of this branch of the healing art. He should not be a historian who presents merely an aggregation of facts, but one who realizes that "it is by solidity of criticism rather by plenitude of erudition that the study of history steadies and straightens and extends the mind," and that "history rescues us from the temporary and the transient and compels us to fasten on abiding issues."

The method of treatment known as osteopathy began with the relief given to one patient and was then applied to others, with what relative success we shall never know for no failures were reported, yet the true scientist thinks "error treated thoroughly nearly as remunerative as truth, by the discovery of new objections." From those inadequately studied cases, wide inductions were drawn concerning the origin or cause of disease and its treatment. The variations in the scope of the inductions are in part responsible for the variations in the definitions of osteopathy.

Osteopathy is a mechanical and kinetic theory of disease, in that impairment of the rate of flow of nerve impulses — later views also included blood and lymph flow — is judged to produce disease. Such impairment occurs most frequently when bony structures are close to nerves, as along the spinal column, specifically at the points of emergence of nerve roots, but may occur in other parts of the body. Dislocations of the vertebrae, minimized for contemplation by the term subluxations, are the chief underlying etiologic factors.

In the early enthusiasm, no other cause for disease was recognized or deemed necessary, and no method of treatment except corrective manipulation was applied. Thus, when early legislative recognition was given, it specified that the osteopath should not use drugs, nor should he perform surgical operations. This gives a general definition of osteopathy as a system of treatment: it is a system of corrective manipulation, without the use of drugs and without surgical operations. It is important to keep this fundamental idea in mind, and it is not necessary to ask at this point just what system of corrective manipulation it comprises.

Throughout the years there has occurred a significant shift in thought on the part of many osteopathic physicians, with a breaking down of distinctions to the point of utter confusion. This is exemplified by the testimony in a recent court case in Kansas.* In that state there is one board of examiners issuing licenses "to practice medicine and surgery" and another granting those "to practice osteopathy." In the case referred to, the defendant, licensed by the second board, practiced medicine and surgery, which was held by the

*Osteopathy: "As taught and practiced in the legally incorporated colleges of osteopathy of good repute" construed. Medicolegal Abstracts, Bureau of Legal Medicine and Legislation. *J. A. M. A.* 113:447, 1939.

complainant to be a violation of the law. The defendant had received "a certificate granting him the right to practice osteopathy in the state of Kansas, as taught and practiced in the legally incorporated colleges of osteopathy of good repute." It was suggested by him that osteopathy had abandoned its fundamental opposition to drug therapy and operative surgery, and now includes the use of these things in its system of healing. Furthermore, it is known that reputable schools of osteopathy include courses in these subjects in their curricula.

The court held that the osteopathic act did not authorize licentiates to use drugs in so far as such drugs are given as remedial aids, nor did it authorize them to practice in the general field of operative surgery with surgical implements, but limited them to manipulative surgery. Therefore the court ousted the defendant from the practice of medicine and surgery.

The significance of this incident from the point of view of the definition of osteopathy is that claims were publicly made by a representative osteopathic physician that osteopathy is what a school of osteopathy teaches and that a licentiate authorized to practice osteopathy is authorized by the Kansas law to practice drug therapy and instrumental surgical therapy, just because reputable schools of osteopathy have enlarged their courses of study to include these subjects. The rejection of this claim by the court is especially welcome because the phrase "as taught in a reputable school" constantly creeps into proposed legislation for branches of the healing art other than osteopathy, and it is often feared, with some justification, that the proposed limits for the license might be gradually and quietly extended to cover a much larger field of practice than was claimed at first.

It may be said in conclusion, that regardless of whatever system of corrective manipulative procedures osteopathy may prove to be on investigation, it has not changed its essence. If it does, it is no longer osteopathy, it becomes something else. It cannot adopt drug therapy or operative instrumental surgery. In a school of medicine in which someone teaches osteopathy, someone may also teach drug therapy or instrumental surgery or even science. Of course, if the law permits, a graduate of an osteopathic school may use drugs if he sees fit, but no matter what any physician may do, osteopathy cannot adopt the principle of drug therapy.

The distinction is of no slight importance because efforts are ever in the making to cloud the issue, to misrepresent "solidity of criticism" as partisan persecution, and always, always, to avoid facing the facts.

CHILD ADOPTION

A RECENT article on adoption by Dr. Douglas A. Thom[1] is well worth consideration, and is of particular interest when considered together with a similar paper by Dorothy Thompson[2] published only a few months previously. One article is fundamentally scientific and appropriately cautious, and the other is distinctly emotional in its appeal; but both arrive at the same basic conclusion.

As stated by Dr. Thom, the conclusion is that "the problem at the moment is not one of getting the perfect child into the perfect home, but rather the broad, sociologic problem of bringing together the largest number of acceptable children and the largest number of acceptable homes, with the objective of increasing the sum total of the satisfactions to be derived by both adoptive parent and child, and with the minimum amount of risk of creating incompatible relationships."

Adoption is obviously a serious business. With this in mind there is a tendency on the part of certain adoption agencies so to safeguard the interests of both child and prospective parents that the difficulties and delays often seem insuperable. It would appear, indeed, to the casual observer that the requirements for adoption are based on considerably higher standards than would obtain for natural children in decent if not *de luxe* strata of society.

As Dr. Thom further says, the problem of bringing together the largest number of acceptable homes and the largest number of acceptable children cannot be satisfactorily settled unless care-

ful investigations are carried out by a group of trained investigators who will determine the obvious reasons why an adoptive procedure would not be successful. From such an investigation could be determined the "reasonable liabilities which must be assumed by both adoptive parents and adoptive child, comparable to the liabilities that invariably occur in the natural parent-child relationship."

In determining the risks involved, it must be remembered that the adoptive parents must make many adjustments. The decision for adoption comes as the result of one or more reasons, which may be carefully considered or may be largely emotional. Perhaps usually an excess of the maternal instinct is at work; perhaps the adoption is decided on from a deep-seated sense of duty; perhaps it is used as the last means of saving a marital situation. In any event the motives are apt to be mingled, and the psychological setup is quite different from that which exists in the natural relationship.

As a matter of fact, most adoptions appear to be highly successful arrangements, and it is pertinent for both Dr. Thom and Miss Thompson to raise the query as to why there should not be more of them. Miss Thompson rightly decries the policy, now happily becoming outdated, of sending illegitimate parent and illegitimate child into the world together to share their mutual woe. She shows, unfortunately, a lack of familiarity with some of the real problems associated with the procedure of adoption.

Also of considerable timely interest in this subject, and emphasizing the necessity for careful investigation before adoption, is the recent exposé[3] of certain baby-selling maternity homes. In these both the unmarried mother and the adopting parents are mulcted until the law occasionally catches up with the racket and forces it at least to change its place of business.

REFERENCES

1. Thom, D. A.: Adoptions. *J. Pediat.* 15:258-265, 1939.
2. Thompson, D.: Fit for adoption. *Ladies Home Journal*, May, 1939.
3. Gardner, M.: Traffic in babies. *Collier's*, September 16, 1939.

MEDICAL EPONYM

Beard's Disease

A paper entitled "Neurasthenia or Nervous Exhaustion," which was read by George M. Beard (1839–1883), then lecturer on nervous diseases at the University of New York, before the New York Medical Journal Association, led to the designation of this condition by the name of its author. The article may be found in the *Boston Medical and Surgical Journal* (**80:** 217–221, 1869).

> The morbid condition or state expressed by this term has long been recognized, . . . but the special name *neurasthenia* is now, I believe, for the first time presented to the profession. . . .
>
> I have for some time been in the habit of employing the term *neurasthenia* to express the morbid state that is commonly indicated by the indefinite phrase, nervous exhaustion. . . .
>
> The derivation of the term *neurasthenia* is sufficiently obvious. It comes from the Greek, . . . and . . . being literally interpreted signifies want of strength in the nerve. . . .
>
> In regard to the pathology of neurasthenia we are compelled, in the absence of definite knowledge, to reason from logical probability.
>
> My own view is that the central nervous system becomes dephosphorized, or, perhaps, loses somewhat of its solid constituents; probably also undergoes slight, undetectable, morbid changes in its chemical structure, and, as a consequence, becomes more or less impoverished in the quantity and quality of its nervous force. . . .
>
> Among the special exciting causes of neurasthenia may be mentioned the pressures of bereavement, business and family cares, parturition and abortion, sexual excesses, the abuse of stimulants and narcotics, and civilized starvation, such as is sometimes observed even among the wealthy orders of society, and sudden retirement from business.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE TO STUDY PROPOSALS FOR BUDGETING THE COSTS OF MEDICAL CARE

The following have been selected by the president, Dr. Walter G. Phippen, to serve on the Committee to Study Proposals for Budgeting the Costs of Medical Care: Dr. Thomas H. Lanman, of Boston, chairman; Dr. John M. Birnie, of Springfield; Dr. James C. McCann, of Worcester; Dr. Michael A. Tighe, of Lowell; and Dr. Shields Warren, of Boston. The president, Dr. Phippen, and the secretary, Dr. Alexander S. Begg, are members ex officiis.

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

PUERPERAL SEPSIS TREATED WITH SULFANILAMIDE

Mrs. E. O., a twenty-year-old para II, about thirty-six weeks pregnant, entered the hospital because of discomfort on November 22, 1938. Labor had not commenced.

The family history was essentially negative. She had had measles and whooping cough; the tonsils and adenoids were removed at the age of four; she had had a mastoid operation at the age of five. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted three to four days. Her last period had begun on March 9, making the expected date of confinement December 16. The previous pregnancy terminated in a low-forceps delivery with a normal convalescence. The present pregnancy had been normal.

On admission the temperature was 100.0°F., and the pulse 114, regular and of good volume. She was not conscious of being ill and did not appear to be ill. The blood pressure was 120 systolic, 80 diastolic. The heart sounds were regular and clear; there were no murmurs. The lungs showed good resonance and were clear throughout. The abdomen was enlarged to a size corresponding to the dates. The fetus was in an ROP position, and the fetal heart rate was 132, the sounds being clear and regular. Rectal examination showed a lightly engaged head and a cervix that was not taken up. The pelvis was of the gynecoid type, slightly contracted. The urine examination was negative. A blood Wassermann test was negative.

On November 23, after a twelve-hour labor, the patient was delivered normally of a female child, weighing 5 pounds, 10 ounces. The placenta separated promptly and was expressed intact. The uterus contracted well. The temperature, however, remained elevated through labor, subsequently rising to 101.2°F., with a slightly elevated pulse. The temperature remained at about 101.0°F., and on the evening of November 24 it rose to 104.0, with a pulse of 124, which was of good quality. The fundus was slightly tender; the lochia was not foul.

Blood examination showed a hemoglobin of 75 per cent, a red-cell count of 4,240,000 and a white-cell count of 17,400. The patient was given 40 gr. of sulfanilamide, with an equal amount of sodium bicarbonate, in divided doses on November 24, the same amount on November 25, and 20 gr. on November 26.

The temperature dropped abruptly to normal the morning of November 25, but rose to 103.4°F. in the evening; then it began a gradual decline, reaching normal on December 1. Because of the marked improvement, the patient received no medication after November 26.

She was discharged from the hospital on December 6, with the uterus in good position and well involuted, the vaults clear and a very slight discharge.

Comment. The marked improvement following the use of sulfanilamide is probably an indication that the infection was caused by a hemolytic streptococcus, although there were no blood or uterine cultures to prove or disprove this statement. This patient undoubtedly had the infection when she started in labor, and whether it came from the uterus or from some other source was not determined.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning March 3:

BERKSHIRE

Thursday, March 7, at 4:30 p.m., at the Bishop House of Mercy Hospital, Pittsfield. Common Problems of Neurology: Indications for lumbar puncture. Instructor: T. J. C. von Storch. Harry G. Mellen, *Chairman.*

BRISTOL SOUTH (Fall River Section)

Tuesday, March 5, at 4:30 p.m., at the Union Hospital, Fall River. Gonorrhea in the Female. Instructor: Oscar F. Cox, Jr. Howard P. Sawyer, *Chairman.*

FRANKLIN

Thursday, March 7, at 8:15 p.m., at the Franklin County Hospital, Greenfield. Cardiovascular Disease: Eleven important questions about heart disease and their answers. Instructor: Ashton Graybiel. Halbert G. Stetson, *Chairman.*

HAMPDEN

Thursday, March 7, at 4:00 p.m., at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, and at 8:15 p.m., in the Outpatient Department of the Skinner Clinic, Holyoke Hospital, Holyoke. Cardiovascular Disease: Eleven important questions about heart disease and their answers. Instructor: Samuel A. Levine. George L. Schadt, *Chairman.*

HAMPSHIRE

Thursday, March 7, at 4:15 p.m., in the Nurses' Home of the Cooley Dickinson Hospital, Northampton. Convulsions in Infants and Children: Etiology and treatment. Instructor: R. Cannon Eley. Warren P. Cordes, *Chairman.*

MIDDLESEX SOUTH

Tuesday, March 5, at 4:30 p.m., at the Cambridge Hospital, 330 Mt. Auburn Street, Cambridge. Pneumonia. Instructor: Chester S. Keefer. Dudley Merrill, *Chairman*.

NORFOLK

Thursday, March 7, at 8:30 p.m., at the Norwood Hospital, Norwood. Complications in Obstetrics, Illustrated by Case Histories. Instructor: John Rock. Hugo B. C. Riemer, *Chairman*.

NORFOLK SOUTH

Monday, March 4, at 8:30 p.m., at the Quincy City Hospital, Quincy. Indications for Cesarean Section. Instructor: M. V. Kappius. David L. Belding, *Chairman*.

PLYMOUTH

Tuesday, March 5, at 4:00 p.m., in the Nurses' Home of the Brockton Hospital, Brockton. Syphilis in Pregnancy and the Offspring. Instructor: Rudolph Jacoby. Walter H. Pulsifer, *Chairman*.

SUFFOLK

Thursday, March 7, at 4:30 p.m., in John Ware Hall, Boston Medical Library, 8 Fenway, Boston. Head and Spine Injuries. Instructor: Donald Munro. Reginald Fitz, *Chairman*.

DEATHS

CUSHMAN — ANDREW B. CUSHMAN, M.D., of South Dartmouth, died February 13. He was in his eighty-fifth year.

Born in Freetown, Massachusetts, he attended the University of Vermont and received his degree from the University of Vermont College of Medicine in 1886.

Dr. Cushman was a fellow of the Massachusetts Medical Society and the American Medical Association, and was a member of the New Bedford Medical Society.

A son and a daughter survive him.

KELLEY — JOSEPH H. H. KELLEY, M.D., of Dorchester, died February 18. He was in his sixty-fourth year.

Born in Boston, he graduated from Tufts College and received his degree from Tufts College Medical School in 1898.

Dr. Kelley was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a daughter and a sister survive him.

MURRAY — GEORGE A. MURRAY, M.D., of South Boston, died January 21. He was in his fifty-sixth year.

Born in Boston, he attended Boston College and received his degree from Harvard Medical School in 1915. For several years before and after the World War he was associated with the Mayo Clinic in Rochester, Minnesota. He was a former member of the Massachusetts Medical Society and the American Medical Association.

His widow, a daughter, a son, a brother and a sister survive him.

PEIRCE — GEORGE A. PEIRCE, M.D., of Enfield, New Hampshire, died February 21. He was in his sixty-sixth year.

Born in Boston, he attended Boston Latin School and received his degree from Harvard Medical School in 1898. Dr. Peirce was formerly the assistant superintendent at the Massachusetts State Infirmary at Tewksbury, but retired five years ago.

He was a member of the Massachusetts Medical Society, the American Medical Association and the New England Society of Psychiatry.

A son and a daughter survive him.

VICKERY — HERMAN F. VICKERY, M.D., of Brookline, died February 22. He was in his eighty-fifth year.

Born in Rochester, New York, he attended Harvard University and received his degree from the Harvard Medical School in 1882. He studied at the University of Leipzig and also served in the Vienna General Hospital. He began practice in Boston and became an instructor of clinical medicine at the Harvard Medical School. Dr. Vickery was physician to the outpatients at the Massachusetts General Hospital from 1885 to 1898, and visiting physician from 1898 to 1914, when he was appointed to the consulting board.

He was a fellow of the Massachusetts Medical Society and the American Medical Association, and was a member of the Boylston Medical Society and the Association of American Physicians.

His widow, two daughters and a son survive him.

MISCELLANY

MAINE NEWS

NEW LICENSEES

The Board of Registration of Medicine lists the following physicians as licensed through examination, as of November 15, 1939:

Karl V. Anderson, M.D. (Tufts '39), Lewiston.
Samuel Bachrach, M.D. (Tufts '38), Worcester, Massachusetts.
Kenneth C. Banting, M.D. (Western Ontario '32), Elmira, New York.
Henry A. Brann, M.D. (Boston University '39), Augusta.
Dexter Clough, 2nd, M.D. (Pennsylvania '39), Bangor.
Paul E. Floyd, M.D. (Harvard '39), Portland.
Norman Jackson, M.D. (Albany '39), Lewiston.
John C. Myer, M.D. (Hahnemann '39), Providence, Rhode Island.
Helen Provost, M.D. (Boston University '35), Augusta.
William D. Reid, M.D. (Harvard '09), Newton, Massachusetts.
John E. Smith, M.D. (Vermont '37), Brooklyn, New York.
Cornelia B. Walker, M.D. (Columbia '34), Portsmouth, New Hampshire.
Thomas B. Walker, M.D. (Columbia '33), Portsmouth, New Hampshire.

The following were licensed through reciprocity:

Wilfred J. Comeau, M.D. (Harvard '33), Boston.
Bernard Diamond, M.D. (Edinburgh '37), Brooklyn, New York.
Henry B. Finks, M.D. (Vermont '37), Portland.
Byron M. Harman, M.D. (Pennsylvania '17), Verona, New Jersey.
Milton S. Thompson, M.D. (Harvard '31), Boston.

REMOVAL NOTICES

The following removal notices have been received:

W. H. Kelly, M.D., from Biddeford to Waterboro.

L. A. Parella, M.D., from Lewiston to North Haven, Connecticut.
G. W. R. Bowie, M.D., from Rangeley to New Gloucester.
R. E. Williams, M.D., from New Gloucester to Freeport.
E. D. Humphreys, M.D., from Jackman to Pittsfield.

MAINE MEDICAL ASSOCIATION

The following physicians have been recently admitted to membership in the Maine Medical Association:

Gordon N. Johnson, M.D., Portland.
Philip Gregory, M.D., Boothbay Harbor.
Clarence J. Kenney, M.D., Togus.
Herbert T. Clough, Jr., M.D., Bangor.
Richard T. Munce, M.D., Bangor.
Walter L. H. Hall, M.D., Old Town.

RHODE ISLAND NEWS

WALTER LEE MUNRO

We think of the late Dr. Walter Lee Munro, not only as a great doctor, but as a great man — a dynamic and truly unique personality.

Born in Bristol, Rhode Island, in 1857, he came of old Pilgrim stock. Educated in the Bristol schools, he took his A.B. degree at Brown University in 1879 and his M.D. at Harvard University in 1885, and practiced his profession in Providence until the very day of his death. As surgeon to the Rhode Island Hospital and consultant to many other hospitals in Providence and throughout Rhode Island and as a private physician, with a large practice among people of all nationalities, creeds and social statuses, he served his community well for over fifty years.

Strong but gentle, wise but simple, devoted to his family but sacrificing his personal comfort to the demands of his practice, ever alive to the growth of medical art and a close student of its expanding literature, applying practically what he heard, saw or read, treating his patients, in and out of hospitals, as people, not subjects, he fulfilled well our ideal of the "perfect doctor." He wrote many creditable medical papers and reports, also many fascinating monographs on lay subjects bearing on the past of his alma mater, — Brown University, — the last of these appearing only a month before his death.

A great reader, he retained with clear-cut memory what he read, as also the events of his own long and varied career. An athlete and hunter, a world-wide traveler, a bon vivant, he was, more than all, a friend. Friendship and friendliness were perhaps the outstanding characteristics of this doctor, who loved and was loved by the world. He just could not help being friendly and hospitable. Partial deafness as well as blindness were his lot in later years, but he simply would not let them "get him," and carried on to the last.

In his death, Dr. Munro leaves with us a fine sense of generous manhood, which looked out not in. He was a man, healthy in body, mind and spirit, whose passing, young at eighty-two, finds the world better for his having lived.

H. DE W.

NOTE

Dr. Chester S. Keefer, associate professor of medicine, Harvard Medical School and junior visiting physician and director of the Second and Fourth Medical Services, Boston City Hospital, gave the annual Henry Sewall Memorial Lecture of the Medical Society of the City and County of Denver on January 30. The title was "Hemolytic Streptococcus Infections: Their importance in acute and chronic disease."

CORRESPONDENCE

MASSACHUSETTS DENTAL SOCIETY

To the Editor: A most cordial invitation is extended to the members of the Massachusetts Medical Society to attend the evening program of the Massachusetts Dental Society, which will be held in the Georgian Room, Hotel Statler, Boston, on Wednesday, April 24, at eight o'clock. Dr. Eben J. Carey, dean of Marquette University School of Medicine, Milwaukee, Wisconsin, will speak on "The Mutual Co-operation in National Health by the Public and the Profession in Medicine and Dentistry." Dr. Walter G. Phippen, president of the Massachusetts Medical Society, will speak on "The Attitude of Organized Medicine in Regard to Socialized Medicine."

WILLIAM H. GRIFFIN, *President,*
Massachusetts Dental Society.

106 Marlborough Street,
Boston.

REPORTS OF MEETINGS

GREATER BOSTON MEDICAL SOCIETY

A regular meeting of the Greater Boston Medical Society was held at the Beth Israel Hospital on December 5, with Dr. Max Ritvo introducing Dr. Emil Novak, of Baltimore, who spoke on "Gynecologic Endocrinology and Organotherapy." In view of the fact that intelligent organotherapy must follow a fundamental knowledge of the underlying endocrinology, the speaker first reviewed the physiology of menstruation. He discussed the production of the estrogens, which persist throughout the cycle, by the ripening follicles and that of progesterone, which occurs only in the second half of the cycle, by the corpus luteum.

Dr. Novak then summarized the physiologic effects of the so-called "sex hormones." The estrogens, which are much more universally distributed than progesterone, were described as being fundamentally growth hormones with selective activity on the Müllerian system. Thus, they are responsible for an increased blood supply and maturation of the reproductive tract. They also cause the rhythmic contractility of the uterine musculature and proliferative changes in the breast and are instrumental in the development of secondary sexual characteristics. The best examples of this in the human being are the results observed in functioning endocrine tumors before puberty and after the menopause.

Progesterone, on the other hand, is a much more specific hormone, which appears to be present only following ovulation. Its effect is produced only on endometrium already primed by estrogen and results in the secretory phase, with its increased glycogen content. Indeed, the appearance of the endometrium after the combined action of the two hormones so closely resembles the early decidual reaction of pregnancy that the two conditions are differentiated only with difficulty on that basis alone. It was pointed out that since the corpus luteum is in reality merely a metamorphosed follicle, the close similarity in chemical structure of the two hormones is not surpris-

ing. Further work has served to divide the nebulous "internal secretion of the ovary" into a group of crystalline compounds.

Dr. Novak then discussed the non-pelvic origins of hormones that affect the reproductive organs. He cited the well-known experiments, since the first description of Fröhlich's syndrome, which have resulted in the hypothesis that the pituitary gland, through its gonadotropic hormones, probably has a governing role. The evidence for two separate tropic substances is now almost incontrovertible; one (FSH) stimulates the maturation of the follicle and the other (LSH) causes the luteinization of the ripe follicle. Unfortunately there has been no isolation of either substance of proved purity or measurable activity. Recent experiments, however, seem to indicate that the gonadotropic substance isolated from the urine of pregnant mares is efficacious as a follicle-stimulating hormone.

Another source of physiologically active sex hormones is the urine of pregnant women, which contains anterior-pituitary-like substances (APL) rather than true overflow pituitary hormones. There are also two distinct endocrines here, sometimes called the prolans. Their origin is now proved by tissue culture, as well as by physiological experiments, to be in the trophoblastic shell of the implanted ovum. Any living, active trophoblast with access to the maternal circulation is capable of producing these substances, which Dr. Novak suggested should be called chorionic hormones. These prerequisites for their presence in the maternal blood explain why a positive Aschheim-Zondek test is usually found in cases with chorionepithelioma and why a negative test may be encountered in an inactive tubal pregnancy.

The final substance employed in female organotherapy is testosterone proprionate, one of the androgenic principles which is closely allied structurally to progesterone and the adrenal hormone, desoxycorticosterone. Although the results are still controversial, the effect of testosterone on the endometrium appears to be one of antagonism to estrogen during the first half of the menstrual cycle and of supplementation to progesterone after ovulation.

Dr. Novak then proceeded to a discussion of organotherapy in various female endocrinopathies. The first consideration was that of functional uterine bleeding, which may be such a plague especially at puberty and the menopause. Dilatation and curettage may often check the condition only temporarily, if at all, and patients have been known to go on to exsanguination during such episodes. The cause of the disorder may be primarily one of ovarian dysfunction, due either to the persistence of an unruptured follicle or to the continued development of more than one follicle. The speaker warned that, in the evaluation of any therapy, this disorder is notorious for its spontaneous remissions and self-limited course. The treatment should consider the phase of the reproductive life of the patient and the desire for children. A complete physical examination and a diagnostic dilatation and curettage should always be carried out in order to rule out organic disease as a cause of the metrorrhagia. At the time of the menopause, the use of radium rather than surgery was recommended unless there was some other indication for laparotomy.

In regard to the hormones, the results in no instance proved conclusively that they were of benefit, but Dr. Novak said that sterilization procedures were too radical in the child-bearing age without a previous attempt at conservative treatment. The various progesterone and prolan products should probably be given only at the time of bleeding, after determining that it is not a true menstrual period. Occasionally there is marked alleviation of symptoms and occasionally none, while usually there is moderate relief. Testosterone should probably be administered throughout the cycle after sufficient control periods have been observed. This more frequently gives favorable results, but in large doses may occasionally result in slight and transient masculinization. Its mechanism was postulated as an inhibition of estrogen through the anterior pituitary gland.

In the treatment of metrorrhagia at puberty, Dr. Novak emphasized the desirability of advising the mother of the protracted period of adjustment which often occurs before a spontaneous termination of the condition occurs. If organotherapy fails, repeated dilatations and curettage should be attempted, with radium implantation being reserved only as a last resort. The speaker made the pertinent suggestion that in any case necessitating transfusion, a donor should be selected, if possible, who is three to four months pregnant.

In opening the discussion, Dr. Joseph C. Aub emphasized the importance of an evaluation of the substrate in any undertaking with organotherapy. This is particularly important in those transition periods of puberty and the menopause. In the former phase there is a crescendo development of the gonadal hormones and the substrate is more susceptible to substitution therapy than in the menopausal patient with her decadent hormonal system. Dr. Aub asked Dr. Novak's views on dysmenorrhea.

The discussion was continued by Dr. Max Davis, who warned of the potential dangers in these therapeutic agents and cited cases of masculinization following the use of even small doses of testosterone. He asked Dr. Novak whether he considered it possible to find the secretory phase in an endometrial biopsy from a patient who had not ovulated.

Dr. Samuel L. Gargill was of the opinion that most patients with metropathia hemorrhagica are subnormal physically and nutritionally, particularly in respect to vitamins. In those who have a large leathery thyroid gland similar to that of thyroiditis, and who have a low basal metabolic rate, it has been found beneficial to use thyroid therapy.

Dr. Novak closed the meeting with a discussion of the problems presented by these men. He was entirely in accord with Dr. Aub in regard to the importance of the substrate in causing variable results in organotherapy. In regard to dysmenorrhea, the speaker said that, in certain cases resulting from hypercontractility of the uterus, progesterone might prove helpful through its antagonistic effect on estrogen. This was suggested by its beneficial effects in certain instances of threatened and habitual abortion. He added that there are a certain number of young asthenic girls under the spell of a doting mother whose threshold can be sufficiently elevated by physical and psychical development. The small residue with healthy bodies and minds in whom intelligent organotherapy has failed are the only patients whom Dr. Novak considers worthy of presacral ganglionectomy. Exhaustive attempts at conservative treatment in such cases should include all the antiestrogenic hormones — progesterone, testosterone and the various anterior-pituitary-like substances.

In answer to Dr. Davis, the speaker expressed the opinion that the secretory endometrium follows only ovulation, despite suggestive work of Hisaw which showed prosecretory granules in castrated monkeys treated with estrin. He said that the results of Hamlin, who found pregnandiol at periods other than those following ovulation, were probably due to faulty technic.

Dr. Novak stated that postmenopausal endometrial hyperplasia could be explained on the persistence of some

estrogenic function following the cessation of external signs. The other hypotheses question the possibility of metabolizing sterols, and more recently point toward the adrenal cortex as the possible site of stimulation in such states.

HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on December 12, 1939.

The first case was that of a forty-nine-year-old Viennese diamond setter, who had entered the hospital four months previously with a history of increasing nausea, vomiting and exhaustion, appearing in that order over a period of eighteen months. Physical examination revealed an emaciated man with pigmentation of the skin of the exposed surfaces in the axillae and of the genitalia and of the mucous membranes. The blood pressure was 100 systolic, 60 diastolic. A tentative diagnosis of carcinoma of the stomach, with a question of Addison's disease, was made. During his stay in the hospital, he collapsed during an x-ray examination, when his blood pressure was found to have a systolic value of 70. Recovery followed the intravenous administration of sodium chloride solution. The serum chloride content ranged from 585 to less than 580 mg. per 100 cc. Urine and sputum specimens each showed acid-fast bacilli only once, and then on the same day. X-ray examination of the chest showed no evidence of pulmonary tuberculosis or of calcified lymph nodes in the abdomen. A sodium chloride deprivation test resulted in acute illness, and relief was afforded by the administration of that substance. A diagnosis of Addison's disease was made, and the patient was put on a regimen of the standard high-salt, low-potassium diet, with an additional 10 gm. of sodium chloride daily. Daily intramuscular injections of 10 and later 5 mg. of desoxycorticosterone acetate were given while the patient was in the hospital. He was discharged greatly improved at the end of three months, and was told to return about every three days for injections. The present return to the hospital was for the implantation of desoxycorticosterone pellets, computed to yield a daily dose of 1 or 2 mg., which had been determined as the patient's approximate maintenance requirement. There has been a moderate decrease of the general pigmentation, but areas of increased pigment at the site of the intramuscular injections were noted.

Dr. Soma Weiss, in discussing the case, stated that the latter phenomenon was undoubtedly due to the increased transport of melanin to the hyperemic area caused by the trauma attendant on the injections. He called attention to the unusually low urinary androgen levels persistently found in this patient, who also complained of decreased libido. The question was raised as to the possibility of elevating the level and improving the associated symptoms with the specific substitution therapy employed. In reply to Dr. William C. Quinby's query as to whether the patient was considered to have tuberculosis, Dr. Weiss stated that it is now questionable whether the chronic destruction observed in the adrenal glands of these patients is actually tuberculous in nature. True tubercles, he said, are not found in this condition. Dr. Joseph C. Aub, in elucidating the problem of the urinary androgen secretion, stated that it was becoming generally accepted that the source of these substances is undoubtedly the adrenal gland and that an inhibition of libido is common.

The second case was that of a seventy-two-year-old man who had had for the past year a dull aching epigastric pain occasionally radiating to the shoulder blades, unassociated with meals, usually occurring during the night, and relieved to some extent by alkalies and vomiting. Lately the pain had increased in severity and there had been occasional coffee-grounds vomitus. There was moderate exertional dyspnea, and minimal ankle edema. Six months prior to entry, an x-ray examination showed a questionable ulcer. On admission the blood pressure was 180 systolic, 110 diastolic; there were crackling basal rales and a slightly tender epigastrium. When the patient was unable to take a Sippy diet due to persistent vomiting, Wangensteen drainage was instituted; but the patient appeared to be going downhill. The stools were strongly positive for occult blood, and the red-cell count fell from 3,400,000 to 2,200,000. Surgery was not considered because of the rales, a fever of 101°F. and the x-ray findings of an early bronchopneumonia. After several blood transfusions and the administration of a considerable quantity of parenteral nutrition and electrolytes, the patient improved and was able to tolerate a fourth-week Sippy diet. The serum protein under the above therapy increased from 4.2 to 5.4 gm. per 100 cc., and a laparotomy was performed. At operation there was a small, benign ulcer of the duodenum with marked spasm, and a posterior gastroenterostomy was performed.

Dr. Elliott C. Cutler discussed the problems entailed in this case. In an elderly person, one is too prone to consider all such lesions malignant rather than benign, but on the whole it is a healthy attitude if one does not balk at operation when there is some indication for it. He emphasized the improvement in preoperative management brought about in recent years, which proved so beneficial in this patient. The importance of the maintenance of the electrolyte balance in cases with vomiting and gastric drainage and of the serum protein level in those with starvation were stressed.

The speaker of the evening, Professor A. Baird Hastings, was introduced by Dr. Weiss. His subject was "Tissue Electrolytes." Dr. Hastings stated that the introduction of new technics of study and an improved interpretation of results had merely served to bring closer together the observed values and those expected from an application of the Gibbs-Donnan and other physicochemical laws to the electrolytes of body fluids. These laws do not describe the behavior of tissue electrolytes, however. It was pointed out that analytical data were difficult to obtain, for there are several kinds of tissue and cells cannot be maintained for long in the absence of their natural environment.

As a result of experiments, it has been shown that the tissues and fluids of the body may be classified as systems of different permeabilities. A membrane permeable to anions and cations, but not protein — the capillary wall — could not obtain in tissues without a progressively increasing intracellular pressure, which is not true except in unusual cases and after death. Blood cells are permeable only to anions of small dimension and to water. Tissues in general are normally impermeable both to anions and cations and permeable only to water and un-ionized molecules.

One of the important findings of Dr. Hastings and his co-workers was the striking resemblance in ionic content of tendon to plasma rather than to muscle. In fact the extracellular phase of tissue was found to be much more like that of diluted connective tissue than of an ultrafiltrate.

Studies on experimental edema with an isotonic solution showed the extracellular swelling to be much greater in an alkaline than in an acid or normal medium. There was also some swelling of the cells in an acid or alkaline medium, while dehydration occurred largely in the cellular phase.

HOUSE OFFICERS ASSOCIATION, BOSTON CITY HOSPITAL

At a regular meeting of the House Officers Association of the Boston City Hospital in the Cheever Amphitheater on December 13, 1939, Dr. Richard B. Cattell spoke on "Malignancy of the Large Bowel."

In introduction Dr. Cattell alluded to the great improvement which has taken place in the surgical treatment of these conditions and attributed this largely to a better evaluation of the patients and an improvement in the preoperative management of the cases. He stated that refinements in technic have been less important.

A tabulation of the Lahey Clinic cases of cancer of the large bowel revealed that about 60 per cent of the lesions occurred in the rectum and 40 per cent in various parts of the colon. Only 39 per cent of lesions in the latter location occurred in men, whereas the incidence in the rectum was 56 per cent. The sex incidence in the entire group, therefore, was about equal when due account was taken of the predominance of rectal lesions. In regard to age distribution, it was noted that the percentage of cases occurring in old age — sixty to seventy-nine — was larger in the colonic than in the rectal group. On the other hand, 16 per cent of the large-bowel cancers occurred in those under thirty-nine years of age. Rectal lesions were most frequent from forty to sixty years.

Dr. Cattell then briefly discussed methods of diagnosis. An illustration of the inadequacy of most such procedures is the fact that 30 per cent of patients with cancer of the large bowel have hemorrhoids and 15 per cent of all patients have had operative treatment of this condition within six months of the time of examination. The speaker stated that the protean and non-specific character of the symptoms usually prevents an accurate diagnosis by the history alone, but should always serve to arouse suspicion and lead to a thorough examination. In regard to the physical findings, Dr. Cattell stated that 50 per cent of colonic carcinomas present palpable, abdominal masses, while 54 per cent of the rectal lesions are within reach of the examining finger in a properly conducted examination. The lithotomy position, even in men, was considered the optimum one.

Proctoscopic examination should be carried out in any suspicious case. An adequate preparation is especially desirable when there are polyps, which Dr. Cattell stated occur in almost 3 per cent of the patients. A biopsy may be taken but a negative report by the pathologist should not be given preference over the entire clinical picture, for the superficial portions of malignant adenomas frequently fail to show evidences of cancer. Such endoscopic studies, in addition to a careful physical examination, enable one to make a diagnosis in 75 per cent of the cancerous lesions of the sigmoid and rectum.

Barium and double-contrast enemas should be employed in all suspected cases before ruling out cancer. A certain number must be subjected to laparotomy in the face of negative evidence in all these tests, purely because of a suggestive history. Although 50 per cent of these explorations will be negative, 1 per cent of all cancerous lesions of the large bowel cannot be demonstrated by any diagnostic procedure except exploratory laparotomy.

Dr. Cattell enumerated the early symptoms suggestive of large-bowel cancer. Rectal lesions are prone to have bleeding, discomfort due to tenesmus, and a change of bowel habits, whereas colonic lesions present a change of bowel habits, anemia, and blood and mucus in the stools. Abdominal cramps are present in only 7 per cent of the rectal and sigmoidal carcinomas as compared with 80 per cent of those of the colon. The incidence of abnormal stools decreases from 86 per cent in the lower lesions to 46 per cent in the left colon to 9 per cent in the right colon.

Before discussing the methods and results of treatment, the speaker alluded to the rapid strides made in recent years in the number of so-called operable cases. Whereas only 48 per cent of those seen between 1922 and 1928 were considered operable, the percentage for the past two years has risen to 89 per cent of all diagnosed cases of large-bowel cancer. These cases were no more favorable than formerly, for this is one group of neoplasms whose delay in treatment still continues. Approximately 10 per cent had liver metastases, many of which, however, were not massive. An additional number have their lives prolonged and the majority have their symptoms alleviated to varying degrees. This lack of selection has naturally decreased the percentage of favorable results and cures, but the presence of a few five-year "cures" in ostensibly inoperable patients has made the procedure definitely worthwhile.

During this same ten-year period when the operability has increased almost 100 per cent, the operative mortality has dropped from 36 per cent to 10 per cent for all types of operations. About 6 to 7 per cent of the patients require some type of enterostomy for obstruction, and a cecostomy is usually employed. The operations of choice in the colonic region are a modified Mikulicz procedure, with no intraperitoneal anastomoses, or a two-stage anastomosis and resection. Procedures carried out for rectal and rectosigmoid cancer are more flexible and vary with the case. Abdominoperineal resections in one or two stages are the commonest, with the latter type having been perfected and used extensively. Other types of operations in this region are loop colostomy and perineal resection, and abdominal resection with a permanent colostomy. The gross salvage in carcinoma of the rectum has been 54 per cent and of the colon 44 per cent for all resected cases.

Dr. Cattell also discussed the difficult problem of polyps, with particular reference to the reputedly precancerous, congenital, adenomatous polyps. Single polyps were considered best treated by fulguration through the sigmoidoscope or by sigmoidotomy or colotomy if beyond reach. In the congenital form, all lesions in the rectum are best fulgurated, and an adequate colectomy and ileosigmoidostomy should follow.

Dr. E. E. O'Neil stated that he preferred a primary aseptic anastomosis on right-sided colonic lesions rather than a Mikulicz procedure, on the basis that the former was at least as safe and was better economically for the patient. Dr. Cattell stated that at the Lahey Clinic the Mikulicz type of operation proved to be the safest procedure, and concluded with the statement that any proved procedure familiar to the individual surgeon may give essentially the same percentage of favorable results.

NOTICES

PETER BENT BRIGHAM HOSPITAL

A research conference of the medical staff of the Peter Bent Brigham Hospital will be held in the amphitheater of the hospital on Tuesday, March 5, at 5:00 p.m. Tea will be served at 4:30 p.m.

PROGRAM

Blood and Urine Iodine in Diabetes Insipidus. Drs. H. H. Blotner and H. J. Perkins.

Further Observations on Dynamics of Circulation in Patent Ductus Arteriosus. Dr. E. C. Eppinger.

All interested persons are cordially invited to attend.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a.m.

MEDICAL CONFERENCES

Friday, March 1 — Rational Use of Chemotherapy. Dr. C. A. Janeway.
Saturday, March 2 — Hospital case presentation. Dr. S. J. Thannhauser.
Tuesday, March 5 — Diagnosis and Treatment of Certain Hip Conditions. Dr. J. D. Adams.
Wednesday, March 6 — Hospital case presentation. Dr. Thannhauser.
Thursday, March 7 — The Phenomena of Taste and Smell. Dr. Alexandra Adler.
Friday, March 8 — Indications for Surgery in the Treatment of Peptic Ulcer. Dr. A. W. Allen.
Saturday, March 9 — Hospital case presentation. Dr. Thannhauser.
Tuesday, March 12 — Review of Recent Cancer Literature. Dr. W. M. Shedden.
Wednesday, March 13 — Hospital case presentation. Dr. Thannhauser.
Thursday, March 14 — The Relation of Cancer of the Stomach to Pernicious Anemia. Dr. Thomas Fujiwara.
Friday, March 15 — Endocrinology. Dr. Fuller Albright.
Saturday, March 16 — Hospital case presentation. Dr. Thannhauser.
Tuesday, March 19 — Clinicopathological conference. Dr. D. S. King.
Wednesday, March 20 — Hospital case presentation. Dr. Thannhauser.
Thursday, March 21 — Control of Gonococcal Infection. Dr. O. F. Cox.
Friday, March 22 — Psychotherapy. Dr. Donald McPherson.
Saturday, March 23 — Hospital case presentation. Dr. Thannhauser.
Tuesday, March 26 — X-ray demonstration. Dr. Alice Ettinger.
Wednesday, March 27 — Hospital case presentation. Dr. Thannhauser.
Thursday, March 28 — The medical, social and preventive aspects of a selected case. Preceptors and medical students.
Friday, March 29 — Some Observations on Pituitary Adenomas. Dr. M. C. Sosman.
Saturday, March 30 — Hospital case presentation. Dr. Thannhauser.

BOSTON LYING-IN HOSPITAL

The next meeting of the Journal Club will be held on Tuesday, March 12, in the lecture hall of the Boston Lying-in Hospital at 8:15 p.m. Dr. Douglas P. Murphy, of the School of Medicine of the University of Pennsylvania, will present his work on topographic recordings of uterine motility.

CARNEY HOSPITAL

The monthly meeting of the John T. Bottomley Society will be held at the Out-Patient Department of Carney Hospital on Tuesday, March 5, at 11:30 a.m. Dr. Benjamin Riseman will speak on "Vertigo."

Physicians and students are cordially invited to attend.

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, March 6, from 2:00 to 4:00 p.m. Drs. Robert Zollinger and E. S. Emery will speak on "Indigestion."

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday evening, March 5, at 8:15.

Dr. William B. Castle will speak on "The Blood Dyscrasias: An aspect of general medicine." A discussion and question period will follow.

ST. ELIZABETH'S HOSPITAL

The annual meeting of the Carney and St. Elizabeth's Hospital staffs will be held at St. Elizabeth's Hospital on March 7 at 12 o'clock noon. The meeting will be conducted by the staff of the Carney Hospital. The following papers will be presented:

Sulfanilamide Treatment of Appendiceal Peritonitis. Dr. John J. Todd.
Menopausal Bleeding: A review of 100 cases. Dr. Edmund L. Carey.
Simple Methods of Treatment in Fracture of Surgical Neck of Humerus. Dr. John L. Doherty.
Responsibility of the Urologist in Hypertension. Dr. Charles J. E. Kickham.

UNITED STATES MARINE HOSPITAL

A staff meeting of the United States Marine Hospital, Chelsea, will be held at "The Hut," on Friday afternoon, March 8, at 4:00. Dr. Sylvester B. Kelley will talk, his subject being "Injuries to the Urinary Tract."

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held at the nurses' residence on Thursday, March 7, at 7:15 p.m. Drs. Clem McKeon and Richard Wadsworth will present a case of Simmonds' disease.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Lowell	March 1	Albert H. Brewster
Salem	March 4	Harold C. Bean
Haverhill	March 5	William T. Green
Gardner	March 12	Mark H. Rogers
Brockton	March 14	George W. Van Gorder
Worcester	March 15	John W. O'Meara
Pittsfield	March 18	Francis A. Slowick
Northampton	March 20	Garry deN. Hough, Jr.
Fall River	March 25	Eugene A. McCarthy
Hyannis	March 26	Paul L. Norton

AMERICAN BOARD OF INTERNAL MEDICINE, INC.

The American Board of Internal Medicine will conduct oral examinations just previous to the meeting of the American College of Physicians in Cleveland and just in advance of the meeting of the American Medical Asso-

ciation in New York City. Applicants who have successfully passed the written examination and plan to take the oral examination in 1940 should advise the office of the secretary at least six weeks in advance of the date of the examination they desire to take.

The next written examination for 1940 will be given on October 21. Applications for this examination must be filed in the secretary's office by September 1. Application forms may be obtained from Dr. William S. Middleton, secretary-treasurer, 1301 University Avenue, Madison, Wisconsin.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, March 3

Sunday, March 3

4 p.m. Backache. Dr. Frank R. Ober. Free public lecture. Harvard Medical School, amphitheater of Building D.

4 p.m. Surgical Diseases of Bone. Dr. John D. Adams. Illustrated, public, health lecture. Faulkner Hospital auditorium.

Monday, March 4

5 p.m. The Hypothalamus and the Sympathetic Nervous System. Dr. S. Walter Ranson. Edward K. Dunham lecture. Harvard Medical School, amphitheater, Building C.

Tuesday, March 5

*9–10 a.m. Diagnosis and Treatment of Certain Hip Conditions. Dr. John D. Adams. Joseph H. Pratt Diagnostic Hospital.

*11:30 a.m. Vertigo. Dr. Benjamin Riseman. John T. Bottomley Society. Out-Patient Department, Carney Hospital.

*5 p.m. Research conference of the medical staff of the Peter Bent Brigham Hospital.

8:15 p.m. The Blood Dyscrasias: An aspect of general medicine. Dr. William B. Castle. Greater Boston Medical Society. Beth Israel Hospital auditorium.

Wednesday, March 6

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*2–4 p.m. Indigestion. Drs. Robert Zollinger and E. S. Emery. Peter Bent Brigham Hospital.

5 p.m. Hypothalamicohypophysial Relationships. Dr. S. Walter Ranson. Edward K. Dunham lecture. Harvard Medical School, amphitheater, Building C.

Thursday, March 7

*9–10 a.m. The Phenomena of Taste and Smell. Dr. Alexandra Adler. Joseph H. Pratt Diagnostic Hospital.

12 m. Annual meeting of the Carney and St. Elizabeth's Hospital staffs. St. Elizabeth's Hospital.

*5 p.m. Clinicopathological conference. Faulkner Hospital.

7:15 p.m. Clinical conference and meeting of the staff of the New England Hospital for Women and Children.

Friday, March 8

*9–10 a.m. Indications for Surgery in the Treatment of Peptic Ulcer. Dr. A. W. Allen. Joseph H. Pratt Diagnostic Hospital.

5 p.m. The Hypothalamus and Behavior. Dr. S. Walter Ranson. Edward K. Dunham lecture. Harvard Medical School, amphitheater, Building C.

Saturday, March 9

*9–10 a.m. Hospital case presentation. Dr. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

March 1 — Staff meeting. United States Marine Hospital. Page 331, issue of February 22.

March 1–30 — Joseph H. Pratt Diagnostic Hospital. Page 369.

March 2, June 8 and 10 — American Board of Ophthalmology. Page 719, issue of November 2.

March 3 — Free public lecture. Quincy City Hospital. Page 77, issue of January 11.

March 7–9 — New England Hospital Association. Hotel Statler, Boston.

March 8 — Staff meeting. United States Marine Hospital. Page 369.

March 12 — Journal Club of the Boston Lying-in Hospital. Page 369.

March 14 — Pentucket Association of Physicians. 8:30 p.m., Hotel Bartlett, Haverhill.

April 15–17 — American Association for the Study of Goiter. Page 203, issue of February 1.

April 15–19 — New England Health Institute. Page 284, issue of February 15.

April 24 — Massachusetts Dental Society. Page 365.

April 24–26 — Scientific Session. Academy of Physical Medicine. Hotel John Marshall, Richmond, Virginia.

May 10–18 — American Scientific Congress. Page 1043, issue of December 28.

May 13 — United States Pharmacopoeial Convention. Page 202, issue of February 1.

June 7–9 — American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

June 10–14 — American Physicians' Art Association. Page 332, issue of February 22.

October 21 — American Board of Internal Medicine, Inc. Notice above.

District Medical Societies

ESSEX SOUTH

March 6 — Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcus Infections. Dr. Champ Lyons. Lynn Hospital, Lynn.

April 3 — Addison Gilbert Hospital, Gloucester.

May 8 — Annual meeting. Salem Country Club, Peabody.

FRANKLIN

March 12 — Franklin County Hospital, Greenfield.

May 14 — Franklin County Hospital, Greenfield.

HAMPSHIRE

March 13.

May 8.

Meetings are held at 11:30 a.m. at the Cooley Dickinson Hospital, Northampton.

MIDDLESEX EAST

March 20.

May 15.

Meetings are held at 12:15 p.m. at the Unicorn Country Club, Stoneham.

MIDDLESEX NORTH

April 24.

July 31.

October 30.

NORFOLK SOUTH

March 7.

April 4.

May 2.

All meetings, with the exception of one which is usually held at the Quincy City Hospital, are held at the Norfolk County Hospital in South Braintree, at 12 o'clock noon.

PLYMOUTH

March 21 — Goddard Hospital, Brockton.

April 18 — State Farm.

May 16 — Lakeville Sanatorium, Lakeville.

SUFFOLK

March 27 — Scientific meeting. Symposium on Ulcerative Colitis and Diarrheas. Under the direction of Dr. Chester M. Jones.

April 24 — Annual meeting in conjunction with the Boston Medical Library. Election of officers. Program and speakers to be announced later.

May 2 — Censors' meeting. Page 244, issue of February 8.

WORCESTER

March 13 — Worcester Memorial Hospital.

April 10 — Worcester Hahnemann Hospital.

May 8 — Worcester Country Club.

Each meeting begins with a dinner at 6:30 p.m. and is followed by a business and scientific meeting.

BOOKS RECEIVED FOR REVIEW

The New Food, Drug, and Cosmetic Legislation. Vol. VI, No. 1. Law and Contemporary Problems. 182 pp. Durham: Duke University School of Law, 1939. 75c.

Abnormal Speech. E. J. Boome, H. M. S. Baines and D. G. Harries. 162 pp. Cleveland: The Sherwood Press, 1939. $2.50.

Diseases of the Gallbladder and Bile Ducts. Waltman Walters and Albert M. Snell. 645 pp. Philadelphia and London: W. B. Saunders Co., 1940. $10.00.

Injection Treatment of Hernia, Hydrocele, Ganglion, Hemorrhoids, Prostate Gland, Angioma, Varicocele, Varicose Veins, Bursae, and Joints. Penn Riddle. 290 pp. Philadelphia and London: W. B. Saunders Co., 1940. $5.50.

Miss Susie Slagle's. Augusta Tucker. 322 pp. New York and London: Harper & Brothers, 1939. $2.50.

Clinical Toxicology. Clinton H. Thienes. 309 pp. Philadelphia: Lea & Febiger, 1940. $3.50.

Functional Diseases of the Intestines. Gustav Singer. 80 pp. London, New York and Toronto: Oxford University Press, 1939. $2.50.

Manual of Cardiology: Clinical methods and case histories as problems for study. William D. Reid. 364 pp. London, New York and Toronto: Oxford University Press, 1940. $3.50.

Shock: Blood studies as a guide to therapy. John Scudder. 315 pp. Philadelphia, Montreal and London: J. B. Lippincott Co., 1940. $5.50.

Studies from the Rockefeller Institute for Medical Research. Vol. 114. 640 pp. New York: The Rockefeller Institute for Medical Research, 1940. $2.00.

Orthopedic Operations: Indications, technique and end results. Arthur Steindler. 766 pp. Springfield, Illinois, and Baltimore: Charles C Thomas, 1940. $9.00.

Pulmonary Tuberculosis in Adults and Children. James A. Miller and Arvid Wallgren. 193 pp. New York and Edinburgh: Thomas Nelson & Sons, 1939. $3.50.

The Anatomy of the Nervous System: From the standpoint of development and function. Stephen W. Ranson. Sixth edition. 507 pp. Philadelphia and London: W. B. Saunders Co., 1939. $6.50.

BOOK REVIEWS

Asthma. Frank Coke. With the collaboration of Harry Coke. Second edition. 266 pp. Baltimore: The Williams & Wilkins Co., 1939. $4.00.

This, the second edition of Dr. Coke's book, is interesting chiefly because it accentuates the difference in the treatment of bronchial asthma in England and in the United States. It might be suspected that the allergic problems were inherently dissimilar but, except for the absence of ragweed, they are essentially the same. For the first portions of the book much praise is due. The etiology and the signs and symptoms of asthma are clearly and concisely described. Except for the importance given to the sedimentation rate, his examination of cases follows the general rule. In treatment, however, Dr. Coke advocates methods which many American allergists would find difficult to accept.

In discussing the treatment of inhalant sensitivity, he states (page 199): "At the end of a week of daily injections, he [the patient] should be symptom-free and remain so during the remainder of the treatment although it is never possible to give any guarantee of this." In this country, such gratifying, immediate and complete success is the exception rather than the rule.

Regarding the use of morphine in asthma, there has in the past been some controversy; the majority of the workers, however, from Salter in 1880 to Henderson and Rice in 1939, have been against its use. Morphine slows the respiratory rate, reduces tidal volume and makes the reflexes affecting respirations more pronounced, probably reducing the sensitivity of the respiratory cells to carbon dioxide. Dr. Coke states: "I think it is important to give enough morphine when it is used, and should suggest one-third of a grain, but morphine sulphate, 1/4 gr., with atropine sulphate, 1/150 gr., is usually sufficient to break the attack." Undoubtedly this treatment will break an attack, but euthanasia when practiced should be practiced wittingly and not unwittingly by the attendant physician, who only too often explains, post mortem, that the attack was so severe that not even morphine would control it. In skillful hands, in small doses for rare patients, morphine may be useful, but it is not a drug to use indiscriminately in the dosage suggested.

Dr. Coke also advocates the Danysz vaccine for non-specific treatment. This vaccine, made of "all the organisms found growing in the intestine," is used, apparently with great success, for all types of asthma, and also for hay fever due to pollen but not treated with specific pollen extract. In England, a specific vaccine made of *Enterococcus faecalis* has been used by Freeman and by Fleming for the treatment of certain types of intrinsic asthma, and in this country, vaccines of bacteria from the upper respiratory tract have been used by Brown in conjunction with pollen for non-specific treatment in hay fever, but the reviewer is of the opinion that almost all allergists are agreed that such non-specific vaccines are indifferent in effect and variable in result. Dr. Coke also recommends, but less strongly, the use of autohemotherapy, and peptone by mouth and by injection — two methods generally considered of little value.

The use of helium by inhalation, that of epinephrine in oil by subcutaneous injection and that of aminophyllin and sucrose intravenously are not mentioned. The methods given, however safe and successful in the author's hands, are not universally accepted and may, if used unskillfully, be dangerous.

A Handbook on Diabetes Mellitus and Its Modern Treatment. J. P. Bose. Third edition. 272 pp. Calcutta: Thacker, Spink & Co., Ltd., 1939. Rs. 7-8.

This text, intended for the general practitioner and medical student and based on the author's practice in India, includes, in its third edition, a section on blood lipoids, with particular reference to the relation of cholesterol to arteriosclerosis, and a chapter on protamine zinc insulin.

Of special interest is the inclusion of data concerning the chemical nature of the Indian dietary; the author states: "What gout is to the nobility of England, diabetes is to the aristocracy of India." He regards chronic dietary excesses combined with indolent habits as mainly responsible for both. Among 2000 patients, 68.2 per cent were Hindus and only 14.6 per cent Mohammedans, the latter figure being slightly less than that for the incidence of Europeans of his series. These differences he regards as artificial since Mohammedan women are so seldom examined medically. However, in India, as elsewhere, the mortality rate is increasing, and the rise between 1929 and 1934 was much greater among the Mohammedans than among any other group. Thus, in the city of Calcutta the diabetic mortality rate was 5.2 per 1000 in 1929 and 20.7 in 1934.

In treatment, the author's usual practice is to put the patient on one of three diets, according to racial customs, containing 100 gm. of carbohydrate, 80 gm. of protein and 100 gm. of fat. After a week on such a limited diet, the tolerance is determined and, if necessary, insulin given. Then the diet is raised to 30 calories or more per kilogram.

Diseases of the Foot. Emil D. W. Hauser. 472 pp. Philadelphia and London: W. B. Saunders Co., 1939. $6.00.

This book is a praiseworthy piece of bookmaking; it is profusely illustrated, several of the cuts being in color.

The author has devised, and describes, certain appliances and methods of shoe alteration with which his name is associated. He advances certain theories which are not always consonant with common orthopedic practice, mini-

mizing, for example, the value of special exercises for developing and properly balancing the muscles which control the position of the foot in weight bearing — a defeatist attitude which perhaps is not warranted. He places chief reliance on controlling the position of the foot by felt pads and shoe alterations, advising patients to work out their own salvation in locomotion.

Several chapters merit special commendation. In Chapter 3, proper emphasis is given to the fact that the foot is not an isolated organ of locomotion but intimately coordinated with, and influenced by, the mechanics of the body as a whole; the foot in its turn exerts an influence on these same mechanisms. Chapter 4, dealing with the hygiene and general care of the feet, is excellent, as are also Chapter 13 on fractures of the foot and ankle and Chapter 26 on the care of the feet during pregnancy and following prolonged illness. Chapters 27, 28, 29 and 30 on the special technics, including local anesthesia, methods of manipulation and special appliances, are clearly written and will be found to be very useful.

The essential etiology of many foot ills is said to be "functional decompensation"; this may be true, but the proof is not always so clear as the reader might wish. In advocating certain operative methods, it seems as though the debt we owe to such outstanding pioneers as Michael Hoke and H. Winnett Orr should be acknowledged.

The book is an attempt to cover all ills of the human foot from an embryological, anatomical, physiological and etiologic background, and the author — a busy and successful practitioner — describes the treatment that he has found most efficient, an approach to the subject which is certainly practical. The task which he set himself was a hard one; he has evidently labored zealously to fulfil it, but has been taken rather far afield.

Mental Health: Publication of the American Association for the Advancement of Science, No. 9. Edited by Forest R. Moulton and Paul O. Komora. 470 pp. Lancaster, Pennsylvania: The Science Press, 1939. $3.50.

This series of papers on psychiatry and its contributions to medicine and to social welfare is extremely valuable. In a sense the audience, which consisted entirely of guests invited by a critical committee, must be given a large part of the credit for the careful preparation of the summaries which were presented. Propaganda is practically absent. There are only a few instances where pure hope dominates a paper. Almost every contributor presents evidence which indicates an opportunity for better care of mental disease and better use of community resources for the study of mental health in general. The reviewer believes that this volume contains the best summary of psychiatry in relation to the community which is available. Obviously it is not to be used as a textbook, and equally obviously it is not likely to appeal to those who are not already interested.

Diseases of the Skin. Richard L. Sutton and Richard L. Sutton, Jr. Tenth edition. 1549 pp. St. Louis: C. V. Mosby Co., 1939. $15.00.

This edition of an increasingly popular textbook in dermatology is rapidly approaching the status of a single-volumed encyclopedia. Not only are all the common diseases of the skin very thoroughly described from every angle, but even the rare dermatoses are adequately considered. Many of the special chapters are so complete that they are practically monographs on their particular subjects. For example, the chapter on diseases due to fungi, which contains a small table of the characteristics of fungi for laboratory identification by Lewis and Hopper and which consists of 144 pages of material descriptive of fungous infections, is in itself almost worth the price of the entire book. The chapter on syphilis, which consists of about 100 pages and which contains a concise and succinct subchapter on the serodiagnosis of syphilis by Rein, is complete from every standpoint. The chapter dealing with the various diseases due to animal parasites is practically a complete course in parasitology.

All in all, nothing except the highest praise can be given to the authors, who not only have compiled as fine a textbook in dermatology as can be placed within two covers, but also have devised a particularly interesting and unusually attractive method for the citation of references, which form in themselves an almost indispensable adjunct to the library of any dermatologist. There are 1452 illustrations in black and white and 21 in full color. This book should be on the bookshelf of every dermatologist.

Aids to Dermatology and Venereal Disease. Robert M. B. Mackenna. Second edition. 284 pp. Baltimore: The Williams & Wilkins Co., 1939. $1.25.

This small handbook by a well-known dermatologist is unusually complete, clearly readable and well organized. It considers many aspects of a large number of the commoner skin diseases in a succinct form. The format of the book lends itself to quick reference. Although this was published early in 1939, several important contributions which were well established by then were omitted, for example, the so-called "quick" tests for syphilis, such as the rapid Kline and rapid Hinton tests, Marpharsen as an important antisyphilitic drug, and the intradermal test for chancroid using a vaccine of the Ducrey bacillus; these omissions are, however, not very serious for a small book with its limited space.

The book is unusually free from the frequent mention of patent remedies which occurs so commonly in many English and Continental texts. It also lacks the strange sounding descriptive dermatology that is frequently found in books not published in America. Although it has the shortcoming of all small, concise books in its tendency to dogmatism, most of the controversial aspects are fairly well covered. One can, of course, take exception to numerous sentences here and there, such as "X-rays . . . are of considerable therapeutic use in psoriasis." Generally, however, this is a very commendable book, not only for students but for general practitioners, particularly in view of its low price.

The Doctor Prescribes Music: The influence of music on health and personality. Edward Podolsky. 134 pp. New York: Frederick A. Stokes Co., 1939. $1.50.

In these times there is so much to be learned that the average medical man in his unsuccessful effort to keep up to date is swamped by reading material. He attempts to select and choose those subjects which will contribute to his skill. No matter what he reads he attempts to derive information, added thought or some idea which becomes part of his being. The reviewer had hoped for just this when reading Podolsky's book, but found that he doubted a good many of the statements in the text and questioned the interpretations of the effects of music on the physiology of the organism. Although the reviewer prefers to hear music than read about it, he could not see any scientific relation between emotional experiences and the reflexes. There is no tool to measure emotions or sensations or the therapeutic value of an emotional experience